EFFECTS OF HEAD TRAUMA ON HEART RATE, BLOOD PRESSURE, CEREBRAL BLOW FLOW, AND ORTHOSTATIC TOLERANCE

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ABSTRACT

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Contact-sports can elicit concussions, which impacts autonomic function, as well as elicit repetitive head trauma, where autonomic function has not yet been assessed. **Purpose:** To determine if differences in autonomic function exist among three groups (CTRL: healthy non-contact-sport participant; RHT: repetitive head trauma contact-sport participant; CONC: previous concussion). **Methods:** Forty men (16) and women (24), aged 18-37 (22±3), participated. Participants were grouped based on their sport and concussion history (CTRL, RHT, CONC). Body composition was measured via air displacement plethysmography. The participant was outfitted with equipment to evaluate heart rate, blood pressure, and cerebral-artery blood flow velocity (CBFv), as the participant performed three stimuli: deep breathing, Valsalva maneuver, and a 70° head-up tilt test. Following autonomic function testing, a YMCA submaximal cycle test was performed. All group comparisons were analyzed using a one-way ANOVA; all data are presented as means ± standard deviation. **Results:** The groups did not differ in respiratory sinus arrhythmia (CTRL: 22±6bpm, RHT: 21±8bpm, CONC: 19±7bpm; p=0.471), Valsalva ratio (CTRL: 2.19±0.39, RHT: 2.09±0.37, CONC: 2.00±0.47; p=0.519), CBFv (CTRL: 47.74±25.28cm/s, RHT: 40.99±10.93cm/s, CONC: 43.97±17.55cm/s; p=0.657), or tilt time (CTRL: 806.09±368.37sec, RHT: 943.07±339.54sec, CONC: 978.40±387.98sec;

p=0.479). However, CONC (113.24±11.64mmHg) had a significantly higher mean systolic blood pressure during the tilt test than CTRL (102.66±7.79mmHg; p=0.026), while RHT (107.9±9.0mmHg) was not significantly different than CTRL (p=0.39) or CONC (p=0.319).

Conclusion: Concussions may have lasting effects on autonomic function; future studies should control sex. Overwhelmingly, dysautonomia is not present during chronic recovery from concussions or in individuals with RHT from contact-sports.

CHAPTER I

INTRODUCTION

INTRODUCTION

The autonomic nervous system (ANS) involuntarily regulates physiological functions such as heart rate, blood pressure, and blood flow (129). The ANS is controlled by the hypothalamus, brain stem, spinal cord, and the limbic cortex (32) and separated into two divisions: the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) (49, 69). Both the SNS and PNS utilize the vasomotor center to maintain homeostasis by receiving and sending signals from and to target organs (49, 69, 95). These signals are controlled by the stretching of the arteries and right atrium (10, 67).

Baroreceptors in the carotid sinus and aortic arch sense changes in tension and relay this information to the vasomotor center of the brain in order to maintain homeostatic pressure (49, 67). The vasomotor center, via the medulla (113), decreases heart rate and contractility, which results in a decreased arterial pressure (49). Additionally, the stretching of the sinus atrial node in the right atrium as well as the Bainbridge reflex (10) both increase heart rate by sending signal to the heart to increase sympathetic drive and decrease parasympathetic activity (49).

The SNS and PNS both aid in controlling vasomotor signals (2, 49) via sympathetic fibers (101) as well as the vagus nerve to increase and decrease the force and rate of the heart's contractions (49, 69, 101). Dysautonomia, which is impaired autonomic function (63), results when the SNS and PNS cannot maintain homeostasis (125), and affects the regulation of respiration (63), heart rate (63), and exercise tolerance (63).

Autonomic function can be evaluated with minimal discomfort. Cardiovascular reflex pathways are standardly assessed by monitoring beat-to-beat changes in heart rate and blood pressure during deep breathing, the Valsalva maneuver, and a head-up tilt table test (68). In addition to the standard cardiovascular reflex examinations, a bedside assessment can be utilized to evaluate autonomic function. A bedside assessment involves a supine rest followed by a standing upright motion while observe heart rate and blood pressure responses at rest, upon standing, and throughout three minutes of standing (68). Autonomic function testing can be used to assess postural orthostatic tachycardia syndrome and orthostatic hypotension (68), or simply to evaluate an apparently healthy individual.

Concussions have become a topic of interest over the past decade due to their potential lingering effects. Although return-to-play protocols have been established, it can be difficult to diagnose an athlete with a concussion (80, 81), which makes it harder to manage the injury. There have been methods developed in attempt to alleviate this difficulty from athletic trainers, coaches, physicians, and other professionals, however, there is no universally accepted diagnostic criteria (16, 27). If a concussion is not managed and the athlete returns to play too soon, he/she is susceptible to another head injury (21), which requires even more time to recover (6). Returning to play too soon, in addition to the repetitive head trauma often seen in contact-sport athletes, have been speculated to cause permanent damage (87, 90).

Many researchers have used autonomic function testing to evaluate the effects of concussions on the ANS, and it has been suggested that a concussion is associated to dysautonomia. The literature exhibits two distinct time frames of interest: short-term post-concussion (24, 59, 108), long-term post-concussion (53, 54); however, some researchers have also studied a mix of both short- and long-term post-concussion (1, 61, 92). However, none of these studies assess the effects of repetitive head trauma (122) on autonomic function; only one study has been found to address this issue (9).

With the prevalence of concussions being incredibly high in sports (36), and the effects of repetitive head trauma relatively unknown, this area of research is extremely important.

Additionally, the individuals of interest throughout the literature have belonged to either very specific groups, or a combination of all athletic backgrounds. Autonomic function in previously concussed individuals has not yet been compared to autonomic function in individuals who have never been concussed and have either contact-sport or non-contact-sport experience. The information gained from this study can help fill in gaps throughout the literature as well as help direct the next steps in future research.

Study Overview

Statement of the Problem

Concussions and repetitive head trauma effect the autonomic nervous system. However, there is no literature that compares autonomic function of individuals who are exposed to repetitive head trauma to previously concussed and/or not previously concussed individuals. Therefore, this study aims to explore autonomic function in the following three groups:

Control (CTRL): Physically active, but do not participate in contact-sports and never diagnosed with concussion.

Repetitive head trauma (RHT): Participates in contact-sports, but never diagnosed with concussion.

Concussed (CONC): The previously concussed individual. In this group the participant was permitted to be currently experiencing symptoms as long as the concussion occurred three or more months prior to data collection (56, 63).

Hypotheses

The following are the hypotheses for each stimulus:

1. Deep Breathing: The respiratory sinus arrythmia will differ among all groups.
2. Valsalva Maneuver: The Valsalva ratio will be highest in the CTRL group and lowest in the CONC group.
3. Tilt Table Test: Middle cerebral artery blood flow velocity will be the lowest in the CONC group and highest in the CTRL group. Additionally, middle cerebral artery blood flow velocity in the RHT group will be lower than the CTRL group. Also, tilt time will be the longest in the CTRL group and shortest in the CONC group.

Significance

Due to the lack of literature in this area, there is much ambiguity with how concussions and repetitive head trauma affect autonomic function. This study aims to explore autonomic function in both of these groups, as well as compare them to a control group. The goal is to determine if repetitive head trauma has similar affects as concussions on the autonomic nervous system. The information gained from this study will fill in some gaps in literature as well as help direct future research.

Delimitations

1. Participants in the CTRL group have never experienced a concussion in their lifetime and have no contact-sport experience.
2. Participants in the RHT group have never experienced a concussion in their lifetime and have contact-sport experience.
3. Participants in the CONC group experienced a concussion in their lifetime at least three months prior to data collection.

Definition of Terms

Autonomic Dysfunction: The inactivation or excessive activation of the parasympathetic and/or sympathetic activity (125).

Cerebral Autoregulation: Cerebral blood flow remains stable throughout blood pressure variations to maintain homeostasis (7).

Repetitive Head Trauma: The recurrent translational and rotational head acceleration from impact to the head (122).

Physical Activity Readiness Questionnaire (PAR-Q+) (124): Published in 2018 from the collaboration of an expert consensus panel along with experts in the physical activity and prominent health conditions fields (123).

Concussion: "Some people have the misconception that concussions only happen when you black out after a hit to the head or when the symptoms last for a while. But, in reality, a concussion has occurred anytime you have a blow to the head that caused you to have symptoms for any amount of time. These include: blurred or double vision, seeing stars, sensitivity to light or noise, headache, dizziness or balance problems, nausea, vomiting, trouble sleeping, fatigue, confusion, difficulty remembering, difficulty concentrating, or loss of consciousness. Whenever anyone gets a dig or their bell rung, that too is a concussion." This definition was developed in 2013 (107) and validated in 2014 (100).

Contact-Sport: Sports that have a considerable amount of physical contact between opponents that is not incidental, but intentional. Sports that do or do not require physical contact by the structured rules are included (111). E.g.: basketball, soccer, field hockey, lacrosse (men's and women's), wrestling, football, ice hockey, gymnastics, and rugby.

Non-Contact-Sport: Sports that have limited physical contact that is incidental and not required by the rules (111). E.g.: baseball, softball, swimming, track and field, and volleyball.

Organized Sport: A sport that involves officiated/judged competition (100).

Deep Breathing: A test that assesses respiratory sinus arrhythmia, which is the difference in heart rate at the end of expiration and the end of inspiration. The six cycle of inhaling for five seconds then exhaling for five seconds are averaged to calculate respiratory sinus arrhythmia (89).

Valsalva Maneuver: A test that assesses heart rate and systolic blood pressure responses by forced expiration against the resistance of the expiratory pressure, equaling 40 mm Hg. This test lasts 15 seconds (89). The Valsalva ratio is calculated by the longest RR interval in phase IV divided by the shortest RR interval in phase II (131).

Head-up tilt table test: A test that assesses orthostatic tolerance by tilting a table from 180° to 70° to encourage passive standing. The test lasts 20 minutes, or less if pre-syncopal symptoms occur (89). Maximum middle cerebral artery blood flow is collected.

CHAPTER II

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Section I. Autonomic Nervous System

The autonomic nervous system (ANS) contains numerous nerve pathways that function involuntarily to control, maintain, and regulate the body (129). The ANS, which is controlled by the hypothalamus, brain stem, spinal cord and the limbic cortex (32), can also voluntarily work alongside the somatic nerve system (129). The two main divisions that control the ANS and promote homeostasis are the sympathetic nervous system (fight-or-flight) and parasympathetic nervous system (rest-and-digest) (49, 69). In order to maintain homeostasis within the body, visceral organs send signals to autonomic ganglia, the hypothalamus that controls aspects of the vasomotor center, or the brain stem to be controlled by the vasomotor center. However, before a signal can return to a visceral organ, it must travel through both a pre- and post-ganglionic neuron. Only after traveling through the ganglia can the signals return to the visceral organ or enter a new target organ in order to promote maintenance within the body (49, 69, 95).

The Vasomotor Center

The vasomotor center is located in the medulla oblongata and utilizes the glossopharyngeal and vagus nerves to regulate blood pressure and heart rate. The vasomotor center contains lateral portions that transfer excitatory impulses to the heart, via sympathetic fibers (101) that increase the force and rate of the heart's contractions (49, 69). The medial portions, though, decrease force and rate of contraction by delivering signals to the dorsal motor nuclei of the vagus nerve to transfer parasympathetic impulses (49, 101). The type and rate of each signal sent from the vasomotor center can be affected by two main factors: the stretching of the arteries and the stretching of the right atrium.

Baroreceptors, which sense stretches in arteries, are located in the walls of systemic arteries, the carotid sinus, and the aortic arch (49, 67). When stretched, baroreceptors send signals to the central nervous system to attempt to maintain homeostatic pressure. Once the signals reach the medulla (113), secondary signals enter the vasomotor center to inhibit the vasoconstrictor center and excite the vagal parasympathetic center (49, 69). In turn, peripheral veins and arteries vasodilate and heart rate and contractility decreases. The end result is a decreased pressure within the arteries (49, 67).

The stretching of the right atrium is the other physiological process that can control vasomotor center signals. This stretch can directly increase heart rate by 10-15% through the stretch in the sinus atrial node (49). Additionally, the Bainbridge reflex (10) can also increase heart rate by transmitting afferent signals through the vagus nerves to the vasomotor center (10). From there, the vasomotor center sends efferent signals through vagal and sympathetic nerves back to the heart to increase sympathetic drive and decrease parasympathetic activity. This increase in heart rate consequently increases cardiac output in attempt to move the excess blood in heart to the rest of the body (10, 49). In order to control signals sent to and from the vasomotor center, both divisions of the ANS must be utilized to secrete synaptic transmitter substances (2, 49).

Sympathetic Nervous System

The sympathetic nervous system is considered the “fight or flight” division of the ANS and includes pre- and post-ganglionic neurons that innervate the eye, heart, bronchi, liver, stomach, pancreas, intestines, kidneys and adrenal medulla, colon, ureter, bladder, genitalia, sweat glands, and blood vessels (79). The pre-ganglionic neurons are connected to the thoracic and lumber regions of the spinal cord. The post-ganglionic neurons connect to target organs and are synapsed to the pre-ganglionic neurons within sympathetic ganglion chains. These chains are located along both sides of the spinal cord. The pre-ganglionic neuron can choose one of three different ways to travel: synapse to the post-ganglionic neuron in the same spinal cord level, synapse with a post-ganglionic neuron at a different level in the spinal cord, or with multiple post-ganglionic neurons located in different ganglia (79). All 31 pairs of spinal nerves are connected to post-ganglionic neurons of the sympathetic nervous system, which allows for control of target organs near the skin to regulate sweating and vascular smooth muscle tone (79).

There is one effector organ that does not require a signal to travel through a post-ganglionic neuron: the adrenal medulla. While the sympathetic nervous system innervates many effector organs, the adrenal medulla (49, 69) serves a special purpose. An action potential sent from the vasomotor center only has to pass through the pre-ganglionic synapse before entering straight into the adrenal medulla (79). This allows for rapid secretion of epinephrine and norepinephrine into the blood stream from the adrenal medulla. From the blood stream, the epinephrine and norepinephrine enter target organs like the heart to increase stroke volume or the kidneys to increase renin and retention of sodium to control blood pressure (49, 69, 79).

Parasympathetic Nervous System

The parasympathetic nervous system is referred to as the “rest and digest” division of the ANS and includes pre- and post-ganglionic neurons that innervate the eye, face, heart, stomach, colon, intestines, bladder, and genitalia (79). The pre-ganglionic neurons, which are long, are connected to the sacral region of the spinal cord as well as the brainstem. When the nerves from the sacral region exit the central nervous system, they innervate the pelvic cavity. The nerves from the brainstem are the oculomotor, facial, glossopharyngeal, and the vagus nerve. The vagus nerve contains 75% of all parasympathetic fibers (79). The post-ganglionic neurons, which are short and close to or inside the target organs, are synapsed to the pre-ganglionic neurons within terminal ganglia. While the sympathetic nervous system can travel in three different ways, the parasympathetic nervous system effects are localized, straightforward, and discrete (69). In order for the sympathetic and parasympathetic nervous systems to affect a target organ, the ANS utilizes two main neurotransmitters: adrenergic and cholinergic (79).

Adrenergic Neurotransmitters

Adrenergic fibers release norepinephrine, which includes most sympathetic post-ganglionic fibers (79). The adrenal medulla, which is a modified sympathetic post-ganglionic neuron, produces norepinephrine and epinephrine as hormones. In order for epinephrine and norepinephrine to have an effect on the target organ, they must bind to and activate alpha- and beta-adrenergic receptors located on the cell's surface because the neurotransmitters cannot cross the phospholipid bilayer. Therefore, these receptors serve as G protein-coupled receptors, which are second messenger systems that signal physiological change within the cell (79). When norepinephrine is no longer needed, it is taken back into the sympathetic nerve that released it. Additionally, the liver inactivates any surplus circulating norepinephrine and epinephrine (79).

Cholinergic Neurotransmitters

Cholinergic fibers release acetylcholine. These include all pre-ganglionic fibers in the ANS, all post-ganglionic parasympathetic fibers, and sympathetic post-ganglionic fibers that innervate the sweat glands. There are two types of cholinergic receptors that acetylcholine can bind to: nicotinic and muscarinic (79). Post-ganglionic neurons, from both divisions of the ANS, that release acetylcholine can bind to nicotinic receptors to cause an immediate increase of cellular permeability of sodium and calcium ions. Depolarization and excitation of the post-ganglionic neurons is the result of this increase permeability (79). The other receptor is a muscarinic receptor, which is inhibitory or excitatory and must be connected to a G protein-coupled receptor and second messenger system. Post-ganglionic neurons, from some sweat gland-sympathetic neurons and all parasympathetic neurons, that release acetylcholine can bind to muscarinic receptors to signal the second messenger system (79). In order to clear the acetylcholine from circulation after use, enzymatic degradation is utilized to break it into choline and acetate. This process takes approximately one millisecond (79).

Conclusion

If the balance of the sympathetic and parasympathetic nervous system is not functioning correctly, homeostasis will not be maintained and can result in impaired autonomic function known as dysautonomia. Autonomic dysfunction can affect the regulation of respiratory rate (63), heart rate (63), sweating (63), temperature regulation (63), sexual function (63), and gastrointestinal function (63) as well as exercise tolerance (63).

Section II. Evaluation of Autonomic Function

The autonomic nervous system must be evaluated thoroughly in order to diagnose an individual with autonomic dysfunction. First, the individual will complete a health history and physical examination which includes a standard neurological examination (68). Following this, the individual's orthostatic performance will be assessed by measuring blood pressure and heart rate after standing the individual up from a supine rest. Another autonomic response that can be assessed is the individual's heart rate response to deep breathing. During this assessment, heart rate is measured while the individual inhales for five seconds and exhales for five seconds, totaling six breaths per minute (68). In addition to these two assessments, dry oral mucous membranes, vasomotor changes, dry skin and temperature, and peripheral edema in the extremities should be examined (68).

Additionally, there are a couple reliable and objective ways to assess autonomic function. There is a standardized protocol to assess cardiovascular reflex pathways that includes a head-up tilt table test, the measuring of beat-to-beat heart rate response to the aforementioned deep breathing assessment, as well as to the Valsalva maneuver (68). For the majority of individuals with orthostatic hypotension, only five minutes of the tilt test is needed (41). However, some individuals can have delayed orthostatic hypotension, so most researchers agree that a minimum of 10 minutes for the tilt test is necessary to get an accurate measure (89).

After diagnosing an individual as having autonomic dysfunction, a treatment plan should be set into place. The most important action that should take place is educating the individual and his/her family about the condition; heart rate and blood pressure can fluctuate in different situations for someone with autonomic dysfunction, so stabilization interventions should be set in place (68). The following two sections contain definitions of autonomic dysfunction disorders and ways to help manage the disorder.

Orthostatic Hypotension

Orthostatic hypotension involves a drop in blood pressure while changing posture to a standing position If systolic blood pressure is reduced by at least 20 mm Hg or diastolic blood pressure is reduced 10 mm Hg while standing, the individual is diagnosed with orthostatic hypotension (39). If an individual has preexisting hypertension, a drop in systolic blood pressure of 30 mm Hg is more appropriate (39). Orthostatic hypotension can be assessed by a sit-to-stand or during a head-up tilt table test. Upon standing, gravity redistributes the blood within the body to the individual’s legs where 300-800 ml of blood begins to pool. Because the individual is passively standing, vasoconstricting mechanisms must take place to get the blood back to the heart. However, in an individual with orthostatic hypotension, the vasoconstricting mechanisms are inadequate and venous return of the blood is hindered. Therefore, less blood gets back to the heart, the cardiac filling pressure is decreased, and stroke volume and cardiac output are reduced, resulting in cerebral hypoperfusion and inadequate central blood volume (39). Symptoms of orthostatic hypotension include the following: dizziness, lightheadedness, fatigue, leg buckling, weakness, blurred vision, head and neck pain, chest pain, cognitive slowing, orthostatic dyspnea, and on occasion a loss of consciousness can occur (39).

Although orthostatic hypotension is commonly managed via pharmaceuticals, some individuals can manage their symptoms by making lifestyle changes. Daily activities should be planned later in the day because orthostatic hypotension is worse in the morning than in the afternoon due to high supine blood pressure while sleeping, which causes diuresis and loss of blood volume (39). One lifestyle change that is commonly recommended is for the individual to go to sleep with the head of their bed elevated 4-6 inches (68). Additionally, smaller and more frequent meals that are moderate in carbohydrate content should be chosen to avoid postprandial hypotension (39, 68). Individuals should also stand up slowly to avoid cerebral hypoperfusion associated with the fast shifts in central blood volume (68). One last item to take into consideration is monitoring salt and water intake daily to ensure heart rate and blood pressure stay at homeostasis (25, 39).

Postural Orthostatic Tachycardia Syndrome

Postural orthostatic tachycardia syndrome (POTS) involves an increase in heart rate while changing posture to a standing position. To be diagnosed with POTS, heart rate must reach 120 beats per minute or increase by at least 30 beats/minute, along with no orthostatic hypotension (a drop in blood pressure >20/10 mm Hg) upon 10 minutes of standing or tilting (39, 96). Additionally the individuals must experience some the following symptoms for at least six months: lightheadedness, fatigue, weakness of the legs, heart palpitations, visual blurring or tunnel vision, tremulousness, increased ventilation and shortness of breath, exercise intolerance, anxiety, chest and head pain, nausea, coldness or pain in the peripheries, and difficulty concentrating (39, 96). POTS can be assessed with a sit-to-stand or a head-up tilt table test; both tests have the same criteria for diagnosing POTS for adults over 19 years old (39).

The management of POTS is similar to that of orthostatic hypotension. Individuals and their families should be educated on this disorder and should understand how to monitor heart rate and blood pressure (96). Families should be aware that women are four times more likely to experience POTS than men (96) probably due to the decreased orthostatic tolerance seen in healthy females (40). Lifestyle changes like managing diet and physical activity can help control POTS. Eating smaller meals to avoid postprandial hypotension (3), increasing fluid intake to 2 L per day (3, 44), and taking 3-5 g of salt per day in order to help retain fluid, thus increasing overall blood volume (3, 44), have been used with success in the treatment of POTS. Aerobic exercise is also suggested to be completed in 20-30 minute bouts, at least three times per week, along with resistance training to increase venous return form the lower extremities and augment skeletal muscle pump effectiveness (44).

Section III. Concussions

Autonomic dysfunction, and the disorders related to it, have been noted to be associated with concussions. The actual numbers of those cases is unknown and may be larger than reported due to the under reporting (30, 119), missed diagnosis (80, 81), and miscommunication (81) of the head injury (52-55, 63). A concussion is caused by a traumatic biomechanical impact to the head, neck, or face that negatively affects the brain through functional pathophysiological processes (34, 43, 83, 84). Concussions can display prompt neurological impairment without neuroimaging abnormalities, functional neuropathological alterations, clinical symptoms, and cognitive symptoms (84). Upon a head injury, ionic fluxes occur, which causes excessive pumping of the sodium-potassium pump. The pump requires adenosine triphosphate, therefore glucose metabolism spikes, which results in an energy crisis because the supply of glucose is not enough to meet the demand (42). This alteration in glucose metabolism can last up to four weeks (13). Additionally, after a head injury, lactic acid is generated, neurotransmitters are alters, intracellular magnesium is deceased, inflammation occurs, and free radicals are produced (42). The signs and symptoms an athlete experiences after a hit will determine their concussion severity classification (16, 27). Specific symptoms of a concussion are individualized and can be physical, behavioral, and cognitive by the means of headaches, amnesia, slowed reaction times, dazedness, nausea, irritability, depression, and drowsiness (84, 87). Although loss of consciousness (LOC) is included in the symptom list, only 6-9% of concussions are associated with LOC (48, 75, 80).

The standard return to play protocol used to manage an athlete's concussion cannot begin until all symptoms have ceased (50, 51, 87). This occurs after about seven to 10 days in 80-90% of all cases of concussion with no further symptoms persisting (83, 84). If an athlete returns to play too soon, he/she can risk being exposed to second impact syndrome as well as post-concussive syndrome (21, 83, 84, 105). The most important thing to consider when classifying, diagnosing, and managing a concussion is to individually assess and accommodate each athlete (51, 83, 121).

Mild Traumatic Brain Injury

Many researchers and physicians have deemed the term "mild traumatic brain injury" (mTBI) to have the same meaning as the term "concussion" (16, 51, 86, 102), though ambiguity still exists (83). This ambiguity is due, in part, to the nomenclature classifications of a traumatic brain injury (TBI), which has three categories of severity: mild, moderate, and severe. However, only a mTBI encompasses the same symptomology and outcomes as a concussion (16, 51, 86, 102). The Centers for Disease Control and Prevention estimates that of 1.7 million individuals who sustain a TBI, three quarters of the TBIs are classified as mild (36).

Three organizations currently exist that have published diagnostic criteria for classifying a mTBI: The American Congress of Rehabilitation Medicine (ACRM), American Academy of Pediatrics (AAP), and World Health Organization (WHO) (16, 64). Researchers have been working on a way to develop one universally accepted set of criteria to diagnose and treat a concussion (70). As of now, the ACRM, AAP, and WHO criteria are all accepted and used (16, 64).

The ACRM defines a mTBI as any mental alteration at the time of the injury and a LOC that is 30 minutes or less (64). After 30 minutes, a Glasgow Coma Scale (GCS) of 13-15 will be observed (64). The GCS is a scale administered to head trauma patients to determine the severity of the head impact (118). ACRM also states posttraumatic amnesia (PTA) will last no more than 24 hours and no neurological signs will be present for a mTBI (64).

The AAP states that at the time of initial evaluation, mental status will be normal. LOC will occur at some point, but will only last for one minute or less (29). Additionally, there may not be any neurological signs, but seizures, headaches, lethargy, or emesis after the injury may occur (29).

The WHO states that for a mTBI, mental confusion and disorientation can be experienced along with LOC lasting no longer than 30 minutes (22). Unlike the ACRM and AAP, WHO claims there can be abnormalities in transient neurological signs (16, 22, 64). However, positive neuroimaging readings, called “complicated mTBI,” have recently been found to exhibit neurobehavioral and neuropsychological alterations that represent a moderate TBI (117). According to the WHO, a score of 13-15 on the GCS will correlate with 30 minutes following the injury (22). Additionally, PTA can happen up to 24 hours after the injury (22).

Classification

The term “concussion” will be utilized when discussing a mTBI. Both terms encompass the same symptoms and “concussion” is the primary term sports medicine organizations use to describe sports-related head impact (115). To be diagnosed with a concussion, the impact of the head trauma must be assessed first (16). If the trauma is found to be severe or moderate, the individual is diagnosed with a TBI (18, 91). If the trauma is diagnosed as mild using the criteria suggested by ACRM (64) AAP (29), or WHO (22), then the individual can be said to have a concussion (16).

Once a concussion is determined, the severity of the concussion is examined (16). There are three grades that categorize a concussion’s severity: 1, 2, and 3 (16, 27). The three main groups that have established a grading system for concussion severity; they are the Colorado Medical Society (28), the American Academy of Neurology (5), and the Cantu – revised (19). However, there are multiple differences among these guidelines regarding observed symptoms, LOC, and PTA (16, 27).

The Colorado Medical Society (28) states that a grade 1 concussion includes confusion with no LOC or amnesia. A grade 2 concussion also includes confusion and no LOC, but is associated with amnesia. Grade 3 concussions include any head injury that results from a LOC (28). The American Academy of Neurology (5) states that a grade 1 concussion contains transient confusion, no LOC, and symptoms that resolve in less than 15 minutes. Transient confusion, no LOC, and symptoms that resolve in greater than 15 minutes are classified as a grade 2 concussion. Grade 3 concussions include any head injury that results from a LOC (5). The Cantu – revised (19) set of guidelines classifies grade 1 concussions as no LOC and less than 30 minutes of PTA. Grade 2 concussions have LOC for less than one minute, PTA 30 minutes to 24 hours, and symptoms lasting more than 30 minutes but less than seven days. LOC that is one minute or longer, PTA that is 24 hours or longer, and having symptoms for more than seven days are classified as a grade 3 concussion (19).

Although all three classification guidelines are currently used, a recent study found that out of the three criteria previously listed, most (28%) athletic trainers reported they use Colorado Medical Society guidelines (37). Within this group of athletic trainers, more than 18% reported they use a different set of guidelines all together, and many did not use any form of previously created guidelines (37). Therefore, a new set of classification guidelines came out to eliminate grading concussions, which helps with sideline assessment and management (83). The new guidelines state that an athlete is concussed if he/she has abnormalities in one or more of the following clinical areas: concussion symptoms, physical signs, behavioral alterations, cognitive impairments, and/or sleep disturbances (83). Symptoms can include irritability, nausea, drowsiness, amnesia, depression, and slowed reaction times (84, 87), while headache is the most common somatic symptom and feeling foggy or dazed is the most common cognitive symptom (83, 87). Physical signs can include LOC or amnesia, behavioral alterations, cognitive impairments, slowed reaction time, and sleep disturbances (83). Having multiple sets of available classification guidelines creates ambiguity, so one specific set of guidelines should be universally utilized (16, 27).

Under Reporting Concussions

Concussions happen too often to have ambiguous diagnostic criteria (43). According to the Centers for Disease Control and Prevention, the prevalence of sport-related concussions in the United States is 1.6-3.8 million per year (36). Although this is a large number of reported incidents, it is estimated that 50-75% of concussions go unreported (81). A survey of high school football players found that only 47.3% of athletes reported concussion symptoms to their athletic trainer. Upon follow up, the athletes reported that they did not disclose their symptoms because they did not think their injury was serious enough to mention (81). It has also been shown that some athletes intentionally downplay their injuries, hiding symptoms to stay in the game in order to win (30). In one survey, 43% of collegiate athletes momentarily hid concussion symptoms from their athletic trainer to stay in a game (120) and 25% of collegiate athletes from football, basketball, lacrosse, soccer, wrestling, and other sports, admitted to sustaining a head injury throughout their career that went unreported (120). Elite and nonelite ice hockey have also been found to under report concussions (128). Due to the excessive amounts of under reporting and missed diagnoses of concussions, specific sideline criteria should be established to evaluate any head impact an athlete sustains (16, 27, 83).

Sideline Diagnosis

In many cases, concussion signs and symptoms are not immediately experienced, so sideline management during a practice or game can be difficult (35, 80). Therefore, to evaluate a head injury directly following a blow to the head, a general first aid assessment including checking for consciousness and the athlete’s, airway, breathing, and circulation should occur (27, 50, 83). Next, an assessment tool like a symptom checklist (83) or the Sport Concussion Assessment Tool 3 (SCAT3) (47) should be conducted. The SCAT3 is a standardized tool to assess athletes for a concussion which contains the GCS, Maddocks Score to recall an athlete's memory, symptom evaluation, cognitive assessment, neck evaluation, balance examination, coordination examination, and word recall ability (47). Before the SCAT3 (47) was created, the most common way of diagnosing a concussion by professional, collegiate, high school, and certified athletic trainers, was through the use of a symptom checklist (37). However, some concussions present with limited or no symptoms, so in these instances, a symptom checklist is not effective. A study found that of athletic trainers who have access to a neuropsychologist, less than half recommend their athletes to consultations with these professionals due to the lack of or limited symptoms experienced by the athlete (37). Due to the inconsistency of symptoms, a symptom checklist is no longer the most effective way to assess a concussed athlete (26).

After assessments, if the athlete is not diagnosed with a concussion, medical personnel should continue monitoring until the athlete is ready to return to the game or practice; however, once diagnosed with a concussion, the athlete cannot return to play on the same day as the diagnosis (50, 83). Injuries that exceed the SCAT3 assessment tool or symptom checklist should be examined closer; a GCS score less than 15, mental deterioration, potential spinal injury, or worsening of neurological signs and symptoms call for an immediate hospital visit (47).

Management

After the diagnosis of a concussion that does not require hospitalization, the concussion must be managed so the athlete can return to play (RTP) (50). The management of a concussion depends on the duration of symptoms (87). Only after all symptoms are absent should the athlete begin the RTP protocol (50, 51, 87). However, according to the American Medical Society for Sports Medicine, if any symptoms arise once the RTP protocol has begun, the protocol must be stopped and the athlete should return back to the step where he/she was symptom free (51). The

RTP decision is made by athletic trainers in conjunction with physician's recommendation (28.5%), clinical evaluation (24.0%), and RTP guidelines (18.6%) (37).

The current and universally accepted RTP protocol comes from the American Academy of Pediatrics and is separated into six stages (50). The first stage involves no physical activity but allows for symptom limited cognitive activity, which can include playing video games, reading, doing homework, texting, playing trivia or crossword puzzles, or working online (17). Cognitive activity is assessed based on exposure to these activities and is categorized as rest, minimal, moderate, significant, or full cognitive exposure (17). Stage 2 introduces light aerobic exercise at < 70% maximum intensity to increase heart rate, but no resistance training is permitted. Stage 3 includes sport-specific drills with no head impact. Stage 4 allows for non-contact, more complex training drills and progressive resistance training to reintroduce coordination and cognitive aspects. Following stage 4, athletes are reassessed by medical personnel and after full medical clearance, full-contact practices are permitted in stage 5. This stage instills confidence in the athlete and gives an opportunity for the coach to evaluate functional skills. Stage 6 is when the athlete can fully RTP for all practices and games. Each stage should last at least 24 hours and the total RTP protocol should be at least five days (50). This RTP protocol is used internationally and is established as the main RTP protocol (51, 83).

Although a RTP protocol is used in many situations, athletic trainers and coaches should be well informed of the athlete's concussion history as well as concussion signs and symptoms (50, 51, 83, 121). High school and college athletes who are diagnosed with a concussion during the season are three times more likely to experience a second within that same season (46, 48). Additionally, it has been noted that youth athletes are also at an increased risk of future concussions once they have become concussed (34). Therefore, an athlete who has had a history of concussions is more likely to sustain another than an athlete who has never received a concussion (34, 46, 48, 50, 51, 106). Thus, face-to-face interaction and communication with trainers and athletes should be implemented in unison with the RTP protocol performed by an athletic trainer and medical professionals (51, 83, 121).

Second-Impact Syndrome

If a RTP protocol is not followed and the athlete is not treated, the athlete could be at risk for second-impact syndrome (SIS). An athlete of any age who returns to play before fully recovering from his/her concussion and suffers from another head injury, can experience SIS (21, 105). Generally, the athlete will suffer from a second head injury within 10 days of the first one (21). An athlete that is in danger of SIS has returned to play too soon while experiencing symptoms like headache, vision impairments, motor or sensory damages, memory issues, and other cognitive complications (20). 10-15% of concussion symptoms last for at least a week and can persist up to months (83), but concussion symptoms resolution varies ranging from days to months (20, 82, 84). Therefore, the 10-15% of athletes that take longer to recover from a concussion due to persisting symptoms, have greater chances of experiencing SIS (83). Upon the second impact, the athlete experiences symptoms that resemble a grade 1 concussion without loss of consciousness (20). After about one minute, the athlete can experience orthostatic intolerance, but will have dilated pupils, no eye movement, and trouble breathing (20).

SIS can lead to fatal brain swelling that increases intracranial pressure and causes herniation in the temporal lobes and cerebellar tonsils through the foramen magnum. This all cascades to compression of the brainstem (20). Therefore, to avoid SIS, it is suggested that athletes whose symptoms persist beyond 10 days, should incorporate mental, vestibular, and other physical therapies like graded exercise programs into their RTP protocol to avoid premature return to play (83).

Post-Concussive Syndrome

If concussion symptoms are not managed, post-concussive syndrome (PCS) can occur. There are two main organizations that created diagnostic criteria for PCS: The 10th edition of the International Classification of Diseases (130) and the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (6). PCS is defined as experiencing three or more of the following symptoms persisting for at least three months after the injury: fatigue, headache, dizziness, memory problems, irritability, difficulty concentrating, insomnia, and/or intolerance of stress, emotion, apathy or affective disturbance, personality changes, or alcohol consumption (6, 15, 130). If these symptoms worsen after injury and alterations in social and/or occupational functioning occur, reassessment from a medical professional is needed (6, 11, 15). In addition to the symptoms, an individual's brain injury history should be collected and evidence from neurobehavioral testing of cognitive deficits in attention and/or memory must be present (6).

The management of PCS is different than the management of a mTBI. Once diagnosed with PCS, the goal is to improve daily life functioning focusing on the ability to complete acts of daily living. No longer than four weeks should be taken off of work or school to avoid isolation (11). If symptoms continue to persist after attempts to manage them, referral to a multidisciplinary specialized rehabilitation center may be needed (11).

Repetitive Head Trauma

While concussions are generally a result from one blow to the head, some individuals are exposed to many moderate head impacts, which have the potential to accumulate into serious consequences. This repetitive head trauma can occur in any sport or activity that encompasses recurrent head impact that causes translational or rotational head accelerations (122). These head movements are prominent in football, boxing, martial arts, soccer, lacrosse, wrestling, and rugby, along with many other contact-sports. Little research has been conducted in this area; one study examined the effects of repetitive trauma has tied autonomic dysfunction to a group of boxers who were found to suffer from chronically impaired cerebral hemodynamic function, resulting in orthostatic hypotension (9).

Chronic Traumatic Encephalopathy

While most concussed athletes recover within 10 days (83, 84), the recovery process is extended following multiple concussions or repetitive head trauma (34, 87, 106). It has been speculated that an athlete who has experienced multiple concussions may develop chronic traumatic encephalopathy (CTE), which increases the risk for functional and structural brain damage (8, 83, 84). Currently, CTE is only diagnosed after an autopsy. Retrospectively, CTE has been linked to early onset of Alzheimer disease (45), higher rates of neurodegenerative mortality (71), and neurocognitive impairment (114). Recorded symptoms of CTE include the following: depression, suicidal thoughts and, in some, suicide, neuropsychiatric and behavioral problems, poor judgement, emotional instability, and aggressive behaviors (112).

CTE may be more prevalent than what is currently observed due to the post-mortem requirement for diagnosis. Recently a study revealed that 71% of autopsied professional contact-sport athletes had significant signs of CTE and received the post-mortem diagnosis of CTE (65). Additionally, 33% of individuals that played high school football, ages 18 to 52, were diagnosed with CTE following autopsy (90). CTE is a relatively new discovery that has not been extensively researched and diagnostic criteria can be controversial (97, 112).

Conclusion

Overall, concussions and repetitive head trauma can alter the function of pathophysiological processes (9, 34, 43, 83, 84), which can lead to a multitude of symptoms and disruptions in daily acts of living (84, 87). A concussion can be diagnosed by specifically classifying it into grades 1, 2, or 3 depending on the athlete's signs and symptoms (5, 19, 28), or by simply administering a symptom checklist and the SCAT3 (47, 83). Either way, an individualized RTP protocol should begin following the cessation of symptoms and last until the athlete is ready to return to game play (50, 51, 83, 87, 121). If symptoms are not managed or an athlete returns to play too soon, that individual could potentially develop SIS (21), PCS (11), or CTE (83).

Section IV. Current Autonomic Function Research

Concussions (100) have been found to put the autonomic nervous system in jeopardy of malfunctioning; however, the body of research connecting autonomic dysfunction and concussions is limited (1, 24, 53, 54, 59, 61, 92, 108). Current research on concussion's effects on autonomic function can be separated into three groups: short-term post-concussion (24, 59, 108), long-term post-concussion (53, 54), and a mix of short- and long-term post-concussion (1, 61, 92). Studies looking at the short-term effects of a concussion are defined as experiencing a concussion three months or less prior to data collection (78). A concussion occurring longer than three months ago is considered to have long-term post-concussion effects (78).

Short-Term Effects of Concussions

The short-term effects (24, 59, 108) of a concussion on the ANS have been examined more than the long-term effects (53, 54). It has been suggested that the high-frequency heart rate variability component is reduced in concussed athletes (59, 108). This can be explained by a decrease in parasympathetic activity (59). Additionally, the low-frequency/high-frequency ratio was significantly higher in the concussed group than in the control group, implying that the concussed athletes were sympathetic dominant (59). Concussed athletes also experience elevated cerebral blood flow 5-7 days post-concussion (24). The increase in blood flow during the late acute injury period of a concussion is thought to be due to neurovascular inflammation in response to an increased oxygen demand of the damaged and repairing brain tissue (72).

Long-Term Effects of Concussions

Though short-term post-concussive research has been well documented, the long-term post-concussive effects (53, 54) on autonomic function have not yet been established. It has been suggested that patients with a mTBI experience a reduction in their baroreflex sensitivity, possibly due the observed inadequate augmentation of sympathetic and inadequate withdrawal of parasympathetic activity (53). Additionally, respiratory rate, RR intervals, and systolic blood pressure during the Valsalva maneuver test indicated that those with a mTBI experience lower autonomic control at rest and a delayed decrease in blood pressure following the Valsalva maneuver (54).

Short- and Long-Term Effects of Concussions

While the research in this area is sparse, it is also convoluted as some studies include both long- and short-term post-concussion participants, or they do not indicate how long post-concussion the data collection occurred (1, 61, 92). Regardless, it is thought that cerebral autoregulation is impaired during rapid changes in arterial blood pressure following a concussion (61). Additionally, heart rate variability continues to be affected even with a mixed sample of concussed patients (1). With this mixed sample, high frequency bands are reduced, similar to those in the short-term studies, which suggests that these cardiac autonomic modulations may persist with concussion (1).

Additionally, when heart rate variability is assessed in the short-term concussive state and then again in the long-term concussive state, a decrease in the patient's heart rate variability occurs short-term (30 to 40 days). Following this time frame, though, heart rate variability shows a slow increase up to day 75 where then it returns to baseline (92). This suggest an uncoupling between the ANS and cardiovascular systems following concussion (92), indicating that shifts in sympathetic and parasympathetic nervous systems in the concussed patients are impaired (92).

Section V. Conclusion

Although concussions have become a popular topic of interest over the past decade, there are many areas that should be addressed with future research. Understanding the long-term effects mTBIs have on autonomic function should be a priority. Currently, only non-specified individuals (53, 54, 61), professional boxers (9), and a combined sample of contact-sport and noncontact-sport nonprofessional athletes (1, 24, 59, 92, 108) have been assessed. Additionally, there is limited research regarding the influence of repetitive head trauma on autonomic function. Therefore, further research is needed to determine if autonomic dysfunction is associated with long-term exposure to repeated head trauma that is experienced by contact-sport athletes.

CHAPTER III

METHODOLOGY

METHODOLOGY

Study Overview

Sixteen men and 24 women from Ball State University and the Muncie community participated in this study. Participants were screened for age, biological sex, current medications, head injury and sport participation history, smoking status, and physical activity ability. In addition, the individual was screened for known cardiovascular, pulmonary, renal, or metabolic diseases prior to being admitted. Every participant that came to the lab completed the entire data collection process. Upon arrival to the Integrative Exercise Physiology Laboratory, the participant provided both oral and written informed consent (Appendix A) in accordance to the declaration of Helsinki. The participant then completed a Physical Activity Readiness Questionnaire (PAR-Q+) (124) (Appendix B), a head trauma and sport questionnaire (65, 100, 107) (Appendix C), and a symptom checklist (74) (Appendix D) in order to determine the participant's history of head injury and sport participation. Following the paperwork, anthropometrics were measured, instrumentation of autonomic function testing equipment occurred, a Seven-Day Physical Activity Recall (PAR) interview (103) (Appendix E) was conducted, autonomic function testing took place (89, 131), and a YMCA submaximal cycle test was performed.

Procedures

Prior to data collection, Institutional Review Board's (IRB) approval was received from Ball State University. Following this approval, the researcher recruited participants via email (Appendix F), social media (Appendix G), flyers (Appendix H), and word of mouth.

Interested participants were provided the informed consent and screened via email prior to data collection. After availability was determined, the participant visited the Integrative

Exercise Physiology Laboratory on Ball State University's campus for a one-time data collection session lasting ~2-2.5 hours. The participant was asked to fast 12 hours before data collection along with refrain from exercise, caffeine, and alcohol 24 hours before data collection. Additionally, the participant was asked to bring spandex, and a sports bra for women, in order to complete the Bod Pod assessment. In an attempt to minimize the hormonal differences between men and women, data collection for women took place during the early follicular phase of their menstrual cycle (23, 57). For all participants, data collection occurred in the morning to eliminate differences in circadian rhythm (12).

The day of data collection proceeded as follows:

1. Informed consent (3 min)
2. Administer the PAR-Q+ (5 min).
3. Administer the head trauma and sports questionnaire (5-7 min).
4. Administer the symptom checklist (2 min).
5. Anthropometrics: Height, weight, and Bod Pod (15 min).
6. Administer the PAR while Instrumenting the participant (10 min).
7. Check equipment and calibrate (10 min).
8. Baseline measurements (10 min)
9. Begin autonomic function testing.
    a. Deep Breathing (12 min)
    b. Valsalva Maneuver (10 min)
    c. Tilt Test (20 min)
    d. Recovery (5 min)
10. Submaximal YMCA cycle test (15 min)

Participants

Forty men and women, ages 18-37 (22 ± 3), who were apparently healthy (124) and non-smokers, were recruited for this study. The participants were stratified into three different groups (see Table 1):

Control (CTRL): Physically active, but do not participate in contact-sports and never diagnosed with concussion.

Repetitive head trauma (RHT): Participates in contact-sports, but never diagnosed with concussion.

Concussed (CONC): The previously concussed individual. In this group the participant was permitted to be currently experiencing symptoms as long as the concussion occurred three or more months prior to data collection (56, 63).

Table 1. Group characteristics

Group	Male	Female	Previously Concussed (3+ months prior to data collection)	Contact-Sport Experience
CTRL	3	8	No	No
RHT	4	10	No	Yes
CONC	9	6	Yes	Yes/No

CTRL = control group; RHT = repetitive head trauma group; CONC = concussed group.

Instruments and Equipment

Physical Activity Readiness Questionnaire.

The PAR-Q+ was the first document provided to the participant after the informed consent was signed. The purpose of the PAR-Q+ was to effectively and thoroughly collect information on the participant regarding his/her history with physical activity along with medical information that could deter the participant from engaging in physical activity (124). The researcher answered all questions and clarified any terms the participant did not understand on the PAR-Q+. There were no participants excluded because of his/her answers on the PAR-Q+.

Head Trauma and Sport Questionnaire.

The head trauma and sports questionnaire was adapted from previous studies (65, 100, 107). This questionnaire provides definitions for a concussion, contact-sport, non-contact-sport, and organized sport (111). After reading the definitions, the participant recorded the number of previous concussions experienced in his/her lifetime along with the month and year the concussion(s) occurred. Additionally, the participant answered questions regarding the length and frequency of participation in previous and current organized contact- and non-contact-sports. The researcher answered any questions the participant had in order to properly stratify him/her into the correct group.

Symptom Checklist.

The symptom checklist was adapted from a previously established post-concussive symptom checklist (74) by extending the data collection period dates. Only participants who reported a previous concussion filled out this symptom checklist for his/her most recent concussion. The symptoms, which were nausea, vomiting, appetite changes, and unplanned weight loss are all displayed in the participant descriptive characteristics. The researcher answered all questions asked by the participant to clarify definitions.

Anthropometrics.

Height and weight were measured on each participant. A stadiometer was used to measure the participant’s height. Bod Pod (BODPOD, Cosmed, Concord; CA, USA) measured weight and calculated lean- and fat-mass in kilograms while calculating body fat percent via air displacement plethysmography. To prepare for entry into the Bod Pod, the participant was given the exact instructions provided by the Bod Pod manufacturing company (38, 76, 77, 109, 110). Information from the Bod Pod was used to classify body composition.

Physical Activity Recall.

The PAR was developed (103) to assess leisure and occupational physical activity and was conducted because physical activity can affect autonomic function (85, 88). The PAR has been proven to be reliable and valid throughout literature (14, 33, 60, 98, 103, 104, 116). The researcher interviewed the participant according to the script provided in the PAR. To keep the participant focused on the right day and time, the researcher repeated items or phrases on the script as needed. The subjective measures that the participant assigned to each type of physical activity he/she partook in are different intensity levels: moderate, hard, and very hard. These subjective measures correspond to an objective measure, which is the number of calories burned per kilogram of body weight. The calories for the entire week were calculated and then divided by seven to get the average calories burned per day (103).

The PAR was completed by one researcher while the other researcher instrumented the participant with the autonomic function testing equipment. The PAR results are described in the participant characteristics.

Autonomic Function Protocol.

Before autonomic function was assessed, the participant laid in the supine position on a motorized tilt table (Electro Medical Equipment Inc, Marietta; GA, USA), with a pillow supporting the head and a footrest supporting the soles of the feet. The researcher placed electrocardiogram (ECG) electrodes on the participant's right and left chest and one on his/her left abdominal side. The ECG is connected to the Finapres (Finapres Medical Systems B.V., Hogehilweg; Amsterdam, Netherlands) and was used to assess heart rate. Finger photoplethysmography, through a finger cuff placed on the participant's left middle finger, was used to measure beat-to-beat blood pressure and is also connected to the Finapres. To calibrate this finger cuff, a blood pressure cuff, connected to the Finapres, was placed on the participant's right upper arm. A secondary automatic blood pressure cuff (BpTRU Medical Devices, Coquitlam; BC, Canada) was used to confirm changes in blood pressure at rest and during testing in one-minute intervals. To measure cerebral blood flow, the participant was instrumented with a transcranial-Doppler ultrasound 2 MHz probe (Multigon Industries, INC., Elmsford; NY, USA). Once in place, the participant's middle cerebral artery was isonated and the probe secured using an adjustable head band. Lastly, a nasal cannula and pulse oximeter, connected to a capnography pulse oximeter (Nonin Medical, INC., Plymouth; MN, USA), were placed under the participant's nose and on his/her left index or ring finger respectively. LabChart version 8.1.13 (ADINSTRUMENTS, Bella Vista; New South Wales, Australia) was used to collect and analyze the data.

The first stimulus the participant completed was deep breathing to measure cardiac parasympathetic function (89). The participant was instructed to breathe only through the nasal cannula. He/she was instructed to slowly inhale for five seconds, then slowly exhale for five seconds, for a total of six times. After the six breaths, the participant was allowed to breathe normally for three minutes. This was repeated three times. The deep breathing stimulus allowed for the measurement of respiratory sinus arrhythmia (RSA). RSA was calculated by taking the average of the difference in the heart rate, measured by the ECG, at the end of expiration and the heart rate at the end of inspiration for each of the six cycles. RSA normative values are based on the participant's age (89, 131).

The second stimulus was the Valsalva maneuver to measure baroreceptor function. This was accomplished by having the participant forcefully exhale for 15 seconds against a manometer to a minimum of 40 mm Hg. This was repeated three times with three minutes of rest in between each trial. The Valsalva ratio was calculated from the maximum heart rate during the maneuver divided by the lowest heart rate within 30 seconds of the peak heart rate. Normative values for the Valsalva ratio are based on the participant's age (89).

The last stimulus was the head-up tilt table test, which induces orthostatic stress from pooling blood in the lower legs due to passive standing. A motorized table was utilized to raise the participant from supine to 70°. Blood pressure and heart rate were recorded each minute by the ECG, Finapres, and automatic blood pressure cuff. The trans-cranial Doppler measured cerebral blood flow and was monitored for signs of cerebral hypoperfusion. Generally, throughout the test, heart rate should increase 10-30 beats per minute, SBP should not drop more than 30 mm Hg, and mean blood pressure should be less than 20 mm Hg. If the participant experienced any pre-syncopal symptoms (like sweating, blurred vision, nausea, or dizziness), or if the cerebral blood flow indicated cerebral hypoperfusion, with a dramatic increase of heart rate and/or a decrease in systolic blood pressure, the participant was put back down to a supine position and was monitored for five more minutes in recovery. The participant typically recovered from the pre-syncopal symptoms within two minutes after being put back to the supine position. The head-up tilt test lasted 20 minutes or until pre-syncopal signs or symptoms occurred. If the test did not last 20 minutes, it was considered positive (89).

YMCA Submaximal Cycle Test.

Following recovery from the head-up tilt table test, the participant moved to a cycle ergometer (Lode B.V. Medical Technology, Groningen; The Netherlands). A Polar heart rate monitor strap (Polar, Kempele; Finland) was tightened around his/her chest, right under the pectoralis major with the sensor slightly above the xiyphoid process. The chest strap was linked to a Polar watch where heart rate was read and the cycle ergometer seat was adjusted to the participant's hip height. The 15-point categorial 6 to 20 Borg Scale of Perceived Exertion (RPE) was explained to the participant prior to the test. The YMCA submaximal cycle test started at 25 watts. The cycle ergometer was electronically braked to adjust the load based on the participant's revolutions per minute. After three minutes, the participant was asked to estimate his/her exertion using the RPE scale and heart rate was recorded. After the first three-minute stage, the load added to the cycle depended on the heart rate; a higher heart rate meant less load was added. The test was over when the participant's heart rate achieved a minimum of 110 beats per minute in two consecutive stages. Then, the participant performed a three-minute cool down.

Design and Analysis

The purpose of this study was to observe autonomic function amongst three different groups. Descriptive statistics were used to display subject characteristics that include height, weight, body fat percentage, gender, age, concussion status, physical activity level, and symptoms experienced. All statistical analyses were completed using SPSS, version 25 (IBM Corp., Armonk, N.Y., USA). A One-Way ANOVA was conducted and statistical significance was set a priori at $\alpha < 0.05$ to assess differences amongst the three groups. If necessary, a Tukey post hoc analysis was performed.

Chapter IV

RESEARCH JOURNAL MANUSCRIPT

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Research Journal Manuscript

Title: Effects of Head Trauma on Heart Rate, Blood Pressure, Cerebral Blow Flow, and Orthostatic Tolerance

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Running head: Effects of Head Trauma on Autonomic Function

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ABSTRACT

Contact-sports can elicit concussions, which impacts autonomic function, as well as elicit repetitive head trauma, where autonomic function has not yet been assessed. **Purpose:** To determine if differences in autonomic function exist among three groups (CTRL: healthy non-contact-sport participant; RHT: repetitive head trauma contact-sport participant; CONC: previous concussion). **Methods:** Forty men (16) and women (24), aged 18-37 (22±3), participated. Participants were grouped based on their sport and concussion history (CTRL, RHT, CONC). Body composition was measured via air displacement plethysmography. The participant was outfitted with equipment to evaluate heart rate, blood pressure, and cerebral-artery blood flow velocity (CBFv), as the participant performed three stimuli: deep breathing, Valsalva maneuver, and a 70° head-up tilt test. Following autonomic function testing, a YMCA submaximal cycle test was performed. All group comparisons were analyzed using a one-way ANOVA; all data are presented as means ± standard deviation. **Results:** The groups did not differ in respiratory sinus arrhythmia (CTRL: 22±6bpm, RHT: 21±8bpm, CONC: 19±7bpm; p=0.471), Valsalva ratio (CTRL: 2.19±0.39, RHT: 2.09±0.37, CONC: 2.00±0.47; p=0.519), CBFv (CTRL: 47.74±25.28cm/s, RHT: 40.99±10.93cm/s, CONC: 43.97±17.55cm/s; p=0.657), or tilt time (CTRL: 806.09±368.37sec, RHT: 943.07±339.54sec, CONC: 978.40±387.98sec; p=0.479). However, CONC (113.24±11.64mmHg) had a significantly higher mean systolic blood pressure during the tilt test than CTRL (102.66±7.79mmHg; p=0.026), while RHT (107.9±9.0mmHg) was not significantly different than CTRL (p=0.39) or CONC (p=0.319). **Conclusion:** Concussions may have lasting effects on autonomic function; future studies should control sex. Overwhelmingly, dysautonomia is not present during chronic recovery from concussions or in individuals with RHT from contact-sports.

KEY WORDS: Mild traumatic brain injury, athletes, dysautonomia

INTRODUCTION

Concussions have become a topic of interest over the past decade due to their potential lingering effects. Although return-to-play protocols have been established, it can be difficult to diagnose an athlete with a concussion (28, 29), which makes it harder to manage the injury. There have been methods developed in attempt to alleviate this difficulty from athletic trainers, coaches, physicians, and other professionals, however, there is no universally accepted diagnostic criteria (9, 13). If a concussion is not managed well and the athlete returns to play too soon, they are susceptible to another head injury (10), which requires even more time to recover (5). Returning to play too soon, in addition to the repetitive head trauma often seen in contact-sport athletes, has been speculated to cause permanent damage in the autonomic nervous system (ANS) (30, 33).

The ANS involuntarily regulates physiological functions such as heart rate, blood pressure, and blood flow (48) and separated into two divisions: the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) (15, 26). Both the SNS and PNS utilize the vasomotor center to maintain homeostasis by sending and receiving signals from and to target organs (15, 26, 35). These signals are mediated by baroreceptors and the Bainbridge reflex (7, 25) to modulate sympathetic drive and parasympathetic activity in order to maintain homeostasis (15).

The effects of short-term concussions (12, 22, 40), long-term concussions (17, 18), and a mix of both short- and long-term concussions (1, 23, 34) have been assessed throughout literature and have been indicated to affect the autonomic nervous system (ANS). However, none of these studies assess the effects of repetitive head trauma (44) on autonomic function; only one study has been found to address this issue, which observed an increased prevalence of initial orthostatic hypotension in individuals exposed to repetitive head trauma (6).

Therefore, the purpose of this study was to explore autonomic function in the following three groups: Control (CTRL): Physically active, but do not participate in contact-sports and never diagnosed with concussion; Repetitive head trauma (RHT): Participates in contact-sports, but never diagnosed with concussion; Concussed (CONC): Previously concussed three or more months ago. Based on previous literature, we hypothesized that respiratory sinus arrhythmia (RSA) will differ among all groups, the Valsalva ratio will be highest in the CTRL group and lowest in the CONC group, and tilt time will be the longest in the CTRL group and shortest in the CONC group. Additionally, we hypothesized that during the tilt test, middle cerebral artery blood flow velocity (CBFv) will be the lowest in the CONC group and highest in the CTRL group. Also, CBFv in the RHT group will be lower than the CTRL group.

The information gained from this study can add to the growing body of evidence regarding the effects of concussion and repetitive head trauma, and aid the medical community, coaches, athletes, and parents in understanding the effects of long-term concussions and contact-sports on autonomic function.

METHODS

Participants

Sixteen men and 24 women aged 18 - 37 (22 ± 3) from Ball State University and the Muncie community participated in this study. Participants were screened for age, biological sex, current medications, head injury and sport participation history, smoking status, and physical activity ability. Prior to testing, participants were asked to refrain from caffeine, alcohol, and exercise for 24 hours as well as food for 12 hours. Participants were only permitted to drink water *ad libitum* during this time. In an attempt to minimize the hormonal differences between men and women, data collection for women took place during the early follicular phase of their menstrual cycle (11, 20). For all participants, data collection occurred in the morning to eliminate differences in circadian rhythm (8). Means ± standard deviation for participant characteristics are presented in Table 1. The exclusion criteria included having any known cardiovascular, pulmonary, renal, or metabolic diseases, being under the age of 18 yrs or over 40 yrs, taking any medications that alter cardiovascular, pulmonary, renal, or metabolic pathways, smoking, lack of physical ability to complete a submaximal cycle test, a concussion less than three months ago, and refusal to give informed consent. Every participant that came to the lab completed the entire data collection process. The study was approved for completion by the local Institutional Review Board at Ball State University and procedures followed in accordance with the ethical standards of the Helsinki Declaration and was carried out in full accordance to the ethical standards of the International Journal of Exercise Science (31).

Table 1. Participant characteristics

	CTRL	RHT	CONC	P Value
Age (yrs)	21 ± 2	23 ± 2	23 ± 4	P = 0.165
Weight (kg)	66.20 ± 10.06	67.27 ± 12.79	75.43 ±14.50	P = 0.131
Height (cm)	171.7 ± 6.6	167.3 ± 7.8	172.8 ± 9.5	P = 0.181
Body Fat (%)	22.44 ± 8.01	20.38 ± 7.19	20.59 ± 6.89	P = 0.753
Physical Activity Level (kcal/day)	928.40 ± 370.86	1018.15 ± 275.64	1288.22 ± 550.54	P = 0.084
Rel VO_2 max (ml/kg/min)	40.38 ± 11.60	42.21 ± 7.90	37.44 ± 11.33	P = 0.463
Gender (M%/F%)	27%/73%	29%/71%	60%/40%	n/a

Data are presented as means ± standard deviation; CTRL = control group; RHT = repetitive head trauma group; CONC = concussed group; yrs = years; kg = kilograms; cm = centimeters; % = percentage; kcal/day = kilocalories per day; rel VO_2 max = relative maximal oxygen uptake; ml/kg/min = milliliters per kilogram per minute; M% = male percentage; F% = female percentage; n/a = not applicable.

Protocol

Upon arrival to the Integrative Exercise Physiology Laboratory, the participant provided both oral and written informed consent in accordance to the declaration of Helsinki. The participant then completed a Physical Activity Readiness Questionnaire (PAR-Q+) (45), a head trauma and sport questionnaire (24, 37, 39), and a symptom checklist (27) in order to determine the participant's history of head injury and sport participation. Following the paperwork, anthropometrics were measured, instrumentation of autonomic function testing equipment occurred, a Seven-Day Physical Activity Recall (PAR) interview (38) was conducted, autonomic function testing took place (32), and a YMCA submaximal cycle test was performed (2).

Air Displacement Plethysmography: Prior to the body composition assessment, height was measured using a stadiometer without shoes and to the nearest mm (Novel Products Inc., IL, USA). Body composition was assessed by the Bod Pod (Life Measurement Inc., Concord, CA, USA) per manufacturer's instructions.

Head Trauma and Sport Questionnaire: The head trauma and sports questionnaire was adapted from previous studies (24, 37, 39). This questionnaire provides definitions for a concussion, contact-sport, non-contact-sport, and organized sport (41) and after reading the definitions, the participant recorded the number of previous concussions experienced in his/her lifetime along with the month and year the concussion(s) occurred. The participant also identified the length and frequency of participation in previous and current organized contact- and non-contact-sports. This questionnaire was utilized to assign each participant to a group; group characteristics are displayed in Table 2.

Table 2. Group characteristics.

Group	Male	Female	Previously Concussed (3+ months prior to data collection)	Contact-Sport Experience
CTRL	3	8	0%	0%
RHT	4	10	0%	100%
CONC	9	6	100%	80%

CTRL = control group; RHT = repetitive head trauma group; CONC = concussed group; % = percentage of individuals within their respective group.

Symptom Checklist: The symptom checklist was adapted from a previously established post-concussive symptom checklist (27) by extending the data collection period dates. Only participants in the CONC group filled this out regarding their most recent concussion. Data collection took place during the "persisting symptoms" time frame of the symptom checklist. The symptoms, which were nausea, vomiting, appetite changes, and unplanned weight loss are all displayed in Table 3.

Table 3. Symptom recall for most recent concussion.

Symptoms	48hrs Post-Concussion	3-14 days post-concussion	15 days through 1 month post-concussion	2-3 months post-concussion	Persisting symptoms
Nausea	None: 20% Mild: 40% Mod: 27% Sev: 13%	None: 40% Mild: 53% Mod: 7% Sev: 0%	None: 87% Mild: 13% Mod: 0% Sev: 0%	None: 100% Mild: 0% Mod: 0% Sev: 0%	None:100% Mild: 0% Mod: 0% Sev: 0%
Vomiting	None: 80% Mild: 13% Mod: 7% Sev: 0%	None: 93% Mild: 7% Mod: 0% Sev: 0%	None: 100% Mild: 0% Mod: 0% Sev: 0%	None: 100% Mild: 0% Mod: 0% Sev: 0%	None: 100% Mild: 0% Mod: 0% Sev: 0%
Appetite Changes	None: 27% Mild: 27% Mod: 33% Sev: 13%	None: 53% Mild: 27% Mod: 20% Sev: 0%	None: 87% Mild: 7% Mod: 7% Sev: 0%	None: 87% Mild: 13% Mod: 0% Sev: 0%	None: 100% Mild: 0% Mod: 0% Sev: 0%
Unplanned Weight Loss	None: 93% Mild: 7% Mod: 0% Sev: 0%	None: 93% Mild: 7% Mod: 0% Sev: 0%	None: 93% Mild: 7% Mod: 0% Sev: 0%	None: 100% Mild: 0% Mod: 0% Sev: 0%	None: 100% Mild: 0% Mod: 0% Sev: 0%

Data displayed as percentage of participants that experienced the symptom during that specific time frame. Hrs = hours; mod = moderate; sev = severe.

Autonomic Function Testing: A motorized tilt table (Electro Medical Equipment Inc, Marietta; GA, USA) was utilized for the participant to lay supine and to tilt to 70°. A 3-lead electrocardiogram (ECG) was used to assess heart rate. A finger cuff placed on the participant's left middle finger was used to measure beat-to-beat blood pressure through finger photoplethysmography (Finapres Medical Systems B.V., Hogehilweg; Amsterdam, Netherlands). An automatic blood pressure cuff (BpTRU Medical Devices, Coquitlam; BC, Canada) was used to confirm changes in blood pressure at rest and during testing in one-minute intervals. Cerebral blood flow was measured using a transcranial-Doppler ultrasound 2 MHz probe (Multigon Industries, INC., Elmsford; NY, USA). Once in place, the participant's middle cerebral artery was isonated and the probe secured using an adjustable head band. Lastly, a nasal canula and pulse oximeter, connected to a capnography pulse oximeter (Nonin Medical, INC., Plymouth; MN, USA), were placed under the participant's nose and on his/her left index or ring finger. LabChart version 8.1.13 (ADInstruments, Colorado Springs, CO, USA) was used to collect and analyze the data.

Heart rate variability (HRV) was assessed and analyzed throughout the entire autonomic function testing using the low frequency/high frequency (LF/HF) ratio. The autonomic function protocol utilized was previously described by Novak (32). The first stimulus completed by the participant was deep breathing, which measures cardiac parasympathetic function (32). The end result was respiratory sinus arrythmia (RSA) which was calculated the average of the difference in the heart rate, measured by the ECG, at the end of expiration and the heart rate at the end of inspiration for each of the six cycles. The second stimulus was the Valsalva maneuver, which measures baroreceptor function. The end result was the Valsalva ratio (VR), which was calculated from the maximum heart rate during the maneuver divided by the lowest heart rate within 30 seconds of the peak heart rate. The last stimulus was the head-up tilt table test, which assesses orthostatic tolerance and induces blood pooling in the lower extremities via passive standing. The participant was raised to 70° for 20 minutes. If any of the following were experienced, the participant was lowered back to the supine position and the test ended early: pre-syncopal symptoms (sweating, blurred vision, nausea, or dizziness) and/or the cerebral blood flow indicated cerebral hypoperfusion along with a dramatic increase of heart rate and/or a decrease in systolic blood pressure. Middle cerebral blood flow velocity (CBFv), mean systolic blood pressure (SBP), and tilt time were the variables analyzed from the tilt test.

YMCA Submaximal Cycle Test: Protocol was performed as described by the American College of Sports Medicine (2) using a cycle ergometer (Lode B.V. Medical Technology, Groningen; The Netherlands) and a Polar heart rate monitor chest strap (Polar, Kempele; Finland).

Statistical Analysis

Data are reported as means ± standard deviation. All data was evaluated using a One-Way ANOVA. If deemed necessary, a Tukey post hoc analysis was performed. All statistics were calculated using SPSS, version 25 (IBM Corp., Armonk, N.Y., USA) and statistical significance was set a priori at $\alpha < 0.05$.

RESULTS

The CONC group had a significantly higher mean SBP (113.24 ± 11.64 mm Hg) during the tilt test than the CTR group (102.66 ± 7.79 mm Hg; $p = 0.026$), while the RHT group (107.9 ± 9.0 mm Hg) was not different than the CTRL ($p = 0.390$) or CONC group ($p = 0.319$). There were no differences among the groups for LF/HF (CTRL: 1.13 ± 0.53, RHT: 1.19 ± 0.49, CONC: 1.20 ± 0.45; $p = 0.927$), RSA (CTRL: 22 ± 6 bpm, RHT: 21 ± 8 bpm, CONC: 19 ± 7 bpm; $p = 0.471$), VR (CTRL: 2.19 ± 0.39, RHT: 2.09 ± 0.37, CONC: 2.00 ± 0.47; $p = 0.519$), CBFv (CTRL: 47.74 ± 25.28 cm/s, RHT: 40.99 ± 10.93 cm/s, CONC: 43.97 ± 17.55 cm/s; $p = 0.657$), or tilt time (CTRL: 806.09 ± 368.37 sec, RHT: 943.07 ± 339.54 sec, CONC: 978.40 ± 387.98 sec; $p = 0.479$).

DISCUSSION

The purpose of this study was to examine the effects that repetitive head trauma and concussions have on the autonomic nervous system. To our knowledge, this was the first study to assess how the autonomic function of individuals with exposure to repetitive head trauma compares to individuals who have experienced concussion a minimum of three months prior to data collection. We found that mean SBP was higher in the CONC group when compared with the CTRL group. However, our hypotheses that all three groups would significantly differ in RSA, VR, CBFv, and tilt time were not supported by the data.

We found that mean SBP during the tilt test was significantly different between the CONC group and CTRL group. The CONC group had a significantly higher mean SBP during the tilt test than the CTRL group, while the RHT group was not significantly different than the CTRL or CONC group. Therefore, in previously concussed adult men and women, SBP seems to be affected upon orthostatic change. Literature has found that SBP increases in individuals with previous concussions (19) upon orthostatic change, which agrees with our findings. Previously concussed individuals have been found to have an increased sympathetic drive at rest, while healthy controls do not (19) and would potentially explain our results. However, it has also been suggested that SBP is higher in males when compared to females over 24 hours (36). Therefore, sex distribution must be considered because 60% of our CONC group were males, while only 27% of the CTRL group and 29% of the RHT group were males.

Our study also found that individuals in the RHT group did not have a significantly different mean SBP than the CTRL and CONC groups. Initial orthostatic hypotension, without reports of presyncope symptoms, has been previously recognized in individuals with exposure to contact-sports and repetitive head trauma (6). However, there is no evidence that this hypotension continues into the steady-state phase of standing (6). Therefore, the findings from our study further helps explain the previous literature.

Our hypothesis for RSA was refuted, which supports the notion that there is no difference in cardiac parasympathetic function among the three groups. Literature shows that individuals recovering from a traumatic brain injury display a significantly lower parasympathetic activity and RSA, and significantly higher sympathetic domain than the healthy controls (47). Therefore, as the recovery phase moves to chronic (three or more months after a concussion), our data is suggesting that concussed individuals may regain autonomic function. In addition, individuals with contact-sport experience do not have negatively affected cardiac parasympathetic function.

Our VR hypothesis was also refuted, which again suggests there is no difference in parasympathetic function based on heart rate among the groups. To our knowledge, there is no literature that assesses the heart rate component during this maneuver in CONC or RHT groups. However, literature does show that in previously concussed individuals (4 – 98 months post-injury) the Valsalva maneuver induces a delayed decrease in blood pressure, indicating sympathetic dominance (18). Our CONC group contained a much wider chronic recovery range (3 – 261 months post-injury), which could have been a reason we did not get similar significant results. Additionally, the VR results display that individuals with contact-sport experience do not have negatively affected parasympathetic function.

Although our hypothesis for CBFv was also refuted, our findings align with a recent study that found that CBFv does not differ between healthy and previously concussed adults (16). This similarity is supported by the notion of cerebral autoregulation, which states that CBFv generally remains stable regardless of alterations in prefusion and/or blood pressure due to the adjustability of vascular resistance (42) and aortic compliance (43). Additionally, our results suggest that individuals with contact-sport experience do not have negatively affected CBFv upon or during an orthostatic stressor.

Our hypothesis for tilt test time was also refuted which suggests no difference in orthostatic tolerance among the three group. Literature has shown that individuals that are more sympathetic dominant are better able to tolerate orthostatic changes than those who are parasympathetic dominant (4). However, when assessing sympathetic dominance via heart rate variability (HRV), there was no difference in low frequency/high frequency (LF/HF) ratio among the three groups, which would explain why the tilt test time was also not different among the three groups. Additionally, no differences in the tilt test time could also be explained by the unaffected CBFv.

There were a couple limitations in this study. One limitation was that, although the participant was asked and reminded to stand still during the tilt test, a couple of them did have movement. Two of the 11 (18%) participants in the CTRL group, one of the 14 (7%) participants in the RHT group, and 7 of the 15 (47%) participants in the CONC group had involuntary movements during the orthostatic challenge. The movement from almost half of the CONC participants during the tilt could play a major factor as to why the group lasted the longest (increased muscle pump activity). Therefore, small voluntary and/or involuntary movements during the tilt test may be a limitation in this study and should be better controlled in future studies (21).

We did not control for the amount of fluid intake in the morning before data collection as participants were allowed water ad libitum. However, we feel that this is acceptable as we documented fluid intake and only 21 participants partook in 1-16 ounces of fluids (4.71 ± 3.47 oz), which has been shown to have limited effects on autonomic function (3, 14, 46). An additional limitation is that most participants were females, which could have resulted in sex differences among the data. However, all females were tested in the early follicular phase of the menstrual cycle (1 - 3 days following the cessation of bleeding) in attempt to minimize hormonal differences between males and females (11, 20). Future studies may want to address sex differences, specifically assessing SBP during an orthostatic challenge.

Additionally, future studies should control for the number of concussions and the time frame at which the concussions occurred. In the present study, the number of concussions ranged from 1 to 9 (3 ± 2 concussions) and data collection took place 3 to 261 (71 ± 61 months) months after their most recent concussion. To our knowledge, this study was the first to assess the long-term effects of concussions and repetitive head trauma on autonomic function, thus, the participants were accepted as long as a concussion occurred at least three months prior to data collection. The severity of the concussion should also be considered in the future. Concussions in the present study were self-reported, so it would be impossible to accurately assign a severity score for each participant. However, the symptom checklist did confirm that none of the previously concussed participants were still experiencing symptoms at the time of data collection (see Table 3). Future studies should require documentation from the diagnosing physician or athletic trainer.

In conclusion, when exposed to an orthostatic challenge, individuals who have previously been concussed seem to have significantly higher mean SBP than healthy adults with no contact-sport experience, indicating that concussions likely have lasting effects on the autonomic nervous system, while repetitive head trauma from contact-sports do not. The remaining results, though, indicate that concussions, once in the chronic recovery phase, as well as repetitive head trauma from contact-sports do not portray dysautonomia. Further studies should include a more specific concussed population, as well as control for fluid intake, movement during the orthostatic challenge, and sex differences.

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Chapter V

Discussion and Conclusion

DISCUSSION AND CONCLUSION

Discussion

This study was the first to evaluate the autonomic function of healthy controls (CTRL), individuals exposed to repetitive head trauma (RHT), and individuals who have been previously concussed (CONC). To be considered for the RHT group, the individuals must have previous or current contact-sport experience, and to be considered for the CONC group, the individuals must have experienced at least one concussion three or more months prior to data collection. The short-term effects of concussions have been studied throughout the literature, thus the present study focused on the long-term autonomic function effects of concussions and compared them to individuals with repetitive head trauma. The intended outcome of this study was to assess the similarities and/or differences in autonomic function between individuals in the RHT and CONC groups, and to compare those findings to those of the CTRL group.

We found that mean systolic blood pressure (SBP) during the tilt test was significantly different between the CONC group and CTRL group. The CONC group had a significantly higher mean SBP during the tilt test than the CTRL group, while the RHT group was not significantly different than the CTRL or CONC group (CTRL 102.66 ± 7.79 mmHg vs RHT 107.9 ± 9.0 mmHg vs CONC 113.24 ± 11.64 mmHg; $p = 0.026$; RHT vs CTRL $p = 0.39$; RHT vs CONC $p = 0.319$). Therefore, in previously concussed adult men and women, SBP seems to be affected upon orthostatic change. These findings support the notion that as a group, CONC do not experience sympathetic adrenergic failure or orthostatic hypotension because they were able to increase their SBP upon orthostatic stress (66). Some previous literature shows that upon orthostatic change, SBP appropriately decreases with syncope symptoms in previously concussed individuals (52, 63). However, one study, found that SBP actually increases in individuals with previous concussions (55) upon orthostatic change, the current study agrees with this finding.

Previously concussed individuals have been found to have an increased sympathetic drive at rest, while healthy controls do not (55) and would potentially explain our results. However, it has also been suggested that SBP is higher in males when compared to females over 24 hours (99). Therefore, sex distribution must be considered because 60% of our CONC group were males, while only 27% of the CTRL group and 29% of the RHT group were males.

Our study also found that individuals in the RHT group did not have a significantly different mean SBP than the CTRL and CONC groups. Initial orthostatic hypotension, without reports of presyncope symptoms, has been previously recognized in individuals with exposure to contact-sports and repetitive head trauma (9). However, there is no evidence that this hypotension continues into the steady-state phase of standing (9). Therefore, the findings from our study further helps explain the previous literature.

We hypothesized that all three groups would significantly differ in respiratory sinus arrhythmia (RSA), Valsalva ratio (VR), cerebral-artery blood flow velocity (CBFv), and tilt time, however, these were not supported by the data.

RSA assesses cardiac parasympathetic functions and is defined as the difference between the end of expiration and end of inspiration in heart rate (89). Our hypothesis was refuted, which supports the notion that there is no difference in cardiac parasympathetic function among the three groups (CTRL 22 ± 6 bpm vs RHT 21 ± 8 bpm vs CONC 19 ± 7 bpm; $p = 0.471$). Literature shows that individuals recovering from a traumatic brain injury display a significantly lower parasympathetic activity and RSA, and significantly higher sympathetic domain than the healthy controls (127). Therefore, as the recovery phase moves to chronic (three or more months after a concussion), our data is suggesting that concussed individuals may regain autonomic function. Our data also suggests, based on the RHT data, that contact-sport experience does not negatively affect cardiac parasympathetic function.

The Valsalva maneuver was another assessment that was conducted to measure parasympathetic function based on heart rate. The VR was calculated from the maximum heart rate during the maneuver divided by the lowest heart rate within 30 seconds of the peak heart rate (89). Our hypothesis was refuted, which again suggests there is no difference in parasympathetic function based on heart rate among the groups (CTRL 2.19 ± 0.39 vs RHT 2.09 ± 0.37 vs CONC 2.00 ± 0.47; $p = 0.519$). To our knowledge, there is no literature that assesses the heart rate component during this maneuver in CONC or RHT groups. However, literature does show that in previously concussed individuals (4 – 98 months post-injury) the Valsalva maneuver induces a delayed decrease in blood pressure, indicating sympathetic dominance (54). Our CONC group contained a much wider chronic recovery range (3 – 261 months post-injury), which could have been a reason we did not get similar significant results. Our data also suggests, based on RHT data, that contact-sport experience does not negatively affect parasympathetic function.

Our hypothesis for CBFv throughout the tilt test was also refuted which suggests there is no difference in CBFv during an orthostatic challenge among the three groups (CONT 47.74 ± 25.28 cm/s vs RHT 40.99 ± 10.93 cm/s vs CONC 43.97 ± 17.55; $p = 0.657$). Literature supports our findings; there is no difference in resting CBFv in recently concussed individuals versus healthy adults (73). Additionally, our data suggests, based on RHT data, that contact-sport experience does not negatively affect CBFv upon and during an orthostatic stressor.

Our hypothesis for tilt test time was also refuted which suggests no difference in orthostatic tolerance among the three groups (CONT 806.09 ± 368.37 sec vs RHT 943.07 ± 339.54 sec vs CONC 978.40 ± 387.98 sec; $p = 0.479$). Literature has shown that individuals that are more sympathetic dominant are better able to tolerate orthostatic changes than those who are parasympathetic dominant (4). However, when assessing sympathetic dominance via heart rate variability (HRV), there was no difference in low frequency/high frequency (LF/HF) ratio (CTRL 1.1334 ± 0.53 vs RHT 1.1946 ± 0.49 vs CONC 1.2048 ± 0.45; $p = 0.927$). These findings suggest that there is no difference in sympathetic dominance among the three groups, which would explain why the tilt test time was also not different among the three groups. Additionally, no differences in the tilt test time could also be explained by the unaffected CBFv.

In order to retrieve the most accurate results from this study, a couple confounding variables were assessed via an ANCOVA to limit bias in autonomic function amongst the three groups. Percent body fat (88, 93, 110), physical activity level (85, 88, 94), and VO_2 max (31, 62) have all been noted to affect autonomic function. However, running ANCOVAs established that these three variables did not have an effect on RSA, VR, and tilt test time. Therefore, the initial results were not influenced by the confounding variables. This suggests that our populations in the CTRL, RHT, and CONC groups had equivalent diversity. See Table 1 for the significance values from the ANCOVAs.

Table 1. P-values for confounding variables

Assessment	Body Fat Percent	Physical Activity Level	Relative VO_2 Max
RSA	0.475	0.704	0.431
VR	0.475	0.640	0.556
Tilt Test Time	0.535	0.628	0.474

All data are presented with significance set at $P < 0.05$. VO_2 Max = relative maximal oxygen uptake; RSA = respiratory sinus arrhythmia; VR = Valsalva Ratio.

There were a couple limitations that were encountered throughout this study. One limitation was that, although the participant was asked and reminded to stand still during the tilt test, a couple of them did have movement. Two of the 11 (18%) participants in the CTRL group, one of the 14 (7%) participants in the RHT group, and 7 of the 15 (47%) participants in the CONC group had slight involuntary movements during the orthostatic challenge. The movement from almost half of the CONC participants during the tilt could play a major factor as to why the group lasted the longest. Therefore, small voluntary and/or involuntary movements during the tilt test may be a limitation in this study and should be better controlled in future studies (58). It is suggested that, in addition to having one researcher monitor and provide feedback to the participant, to record the participant's awareness of the movement.

Another limitation was that we did not control for the amount of fluid intake the in morning before data collection as participants were allowed to have water ad libitum. However, we feel that this is an acceptable limitation because only 21 participants, spread among the three groups, partook in 1-16 ounces of fluids (4.71 ± 3.47 oz). This small amount of fluid has been shown to have limited effects on autonomic function (3, 44, 126). An additional limitation is that most participants were females, which could have resulted in sex differences among the data. However, all females were tested in the early follicular phase of the menstrual cycle (1-3 days following the cessation of bleeding) in attempt to minimize hormonal differences between males and females (23, 57). Future studies may want to address sex differences, specifically assessing SBP during an orthostatic challenge.

There are a couple more limitations that specifically involve the previously concussed sample. The number of concussions when the concussions occurred should both be controlled for in future studies. In the present study, the number of concussions ranged from 1 to 9 (3 ± 2 concussions) and data collection took place 3 to 261 (71 ± 61 months) months after the concussion(s) occurred. This study was the first of its kind to assess the long-term effects of concussions and repetitive head trauma on autonomic function, so as long as the participant experienced a concussion three months before coming in for data collection, he/she was accepted. The severity of the concussion may also want to be considered. In the present study, concussions were self-reported, so it would have been difficult to also assign severity to them. However, the symptom checklist did confirm that none of the previously concussed participants were still experiencing symptoms at the time of data collection. Future studies may want to require documentation from a physician or athletic trainer in attempts to determine concussion severity.

Conclusion

The present study indicates that concussed individuals seem to have significantly higher mean SBP than healthy adults with no contact-sport experience when exposed to an orthostatic stressor, indicating that concussions likely have lasting effects on the autonomic nervous system, while repetitive head trauma from contact-sports do not. However, because this CONC group was male dominant, and males have a higher SBP than females, this could have influenced our results. The remaining results, however, indicate that concussions, once in the chronic recovery phase, as well as repetitive head trauma from contact-sports do not cause dysautonomia.

These findings may add to the growing body of evidence regarding the effects of concussion and repetitive head trauma, and aid the medical community, coaches, athletes, and parents in understanding the effects of long-term concussions and contact-sports on autonomic function.

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APPENDIX A

INFORMED CONSENT

Study Purpose

The purpose of this study is to observe repetitive head trauma and concussions. We will look at how contact-sports effect responses in blood pressure, heart rate, and blood flow.

Inclusion/Exclusion Conditions

Inclusion: Apparently healthy, non-smoking men and women aged 18-40 years. Contact-sport athletes who have had a concussion in the past will be one group. Another group will be contact-sport athletes who never had a concussion. The third group will be non-contact-sport athletes who has never had a concussion. Exclusion: Participants cannot be taking any medicine that effects blood pressure, heart rate, blood flow, heart function, or food digestion.

Participation Procedures and Duration

Autonomic function is how well your body responds to tests. It is measured by looking at changes in blood pressure, heart rate, and blood flow. You will be asked to have not eaten in the 12 hours before data collection. You will also be asked to not exercise, drink caffeine, or drink alcohol in the 24 hours before data collection. You will be reminded of these requirements by email before your data collection date. When you get to the Integrative Exercise Physiology Laboratory (HP 307) for your 2-hour visit, you will complete a symptom checklist to record any problems you currently have. If you are in one of the contact-sport groups, you will then answer some questions about the type of sport(s) you play(ed) and how often/long you play(ed) them. Then, height and weight will be taken. Percent body fat and percent muscle will be measured using a BodPod®. You will take off any jewelry you have and sit quietly for about 2 minutes in a small chamber. To do this, you will wear tight fitting clothing (given to you if needed). Then, you will lay down on your back for 20 minutes. Here, you will be asked questions about your current physical activity. Following the 20 minutes, a 10-ml (<1 Tbsp) blood sample will be collected to look at items in the blood. Next, we will put a small cuff on your fingertip and a plastic tube under your nose. We will also place an object on the side of your forehead and 3 stickers on your chest and stomach. As you do a couple activities, we will watch your breathing, heart rate, brain blood flow, and blood pressure. These activities include breathing exercises, squeezing a device with your hand, and being tilted to an upright position. Then, 5 minutes of recovery will take place while you lay on your back again.

Data Confidentiality or Anonymity

All data will be maintained as confidential (private) and no identifying information such as names will appear in any publication or presentation of the data.

Storage of Data and Data Retention Period

Your information will be stored in a locked filing cabinet in the researcher's office. Password protected electronic files will be stored on a computer in the laboratory and the principal investigator's (the main person overseeing the project) computer. If you are not qualified to participate in this study your information will not be kept. Your information will be destroyed by shredding paper files and permanently deleting electronic information. Additionally, if you withdraw from this study and do not wish to continue, all the data collected will be destroyed and not used in any way.

Risks or Discomforts

All risks involved in the presented study are considered minimal. Risks of blood drawing may include discomfort, bruising, and, in rare instances, infection, lightheadedness, and fainting. We will use clean procedures and trained individuals to make sure that there is minimal discomfort with taking the blood samples.

Sources for Further Help

Emergency medical treatment is available in the event of injury. You will assume responsibility for the costs of medical care that is provided. In the unlikely event of injury or illness of any kind as a result of participation in this research project, Ball State University, its agents and employees will assume whatever responsibility is required by law. Local medical care is available at IU Health – Ball Memorial Hospital (765-747-3111). If treatment is needed, first contact your primary care physician or designated health care professional. If you do not have a PCP, contact a local medical clinic or hospital.

Benefits

The participants may or may not find it beneficial to receive health measures like body fat percentage, blood pressure, and heart rate. You may also benefit from the creation of new scientific knowledge to further head trauma recommendations for healthy men and women.

Voluntary Participation

Your participation in this study is completely voluntary. You are free to withdraw your permission at any time for any reason without penalty or prejudice from the investigator. Please feel free to ask any questions of the investigator before signing this form and at any time during the study.

IRB Contact Information

For questions about your rights as a research subject, please contact the Office of Research Integrity, Ball State University, Muncie, IN 47306, (765) 285-5052 or at orihelp@bsu.edu.

Study Title LONG-TERM EFFECTS OF HEAD TRAUMA IN CONTACT-SPORT ATHLETES ON AUTONOMIC FUNCTION

Consent

I, ___________________, agree to participate in this research project entitled, Long-term effects of head trauma in contact-sport athletes on autonomic function. I have had the study explained to me and my questions have been answered to my satisfaction. I have read the description of this project and give my consent to participate. I understand that I will receive a copy of this informed consent form to keep for future reference.

To the best of my knowledge, I meet the inclusion/exclusion criteria for participation (described on the previous page) in this study.

________________________________ __________________

Participant's Signature Date

Researcher Contact Information

Principal Investigator:

Dr. Andrew T. Del Pozzi,
Exercise Physiology
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APPENDIX B

PHYSICAL ACTIVITY READINESS QUESTIONNAIRE

If you answered NO to all of the questions above, you are cleared for physical activity.
Please sign the PARTICIPANT DECLARATION. You do not need to complete Pages 2 and 3.

- Start becoming much more physically active – start slowly and build up gradually.
- Follow International Physical Activity Guidelines for your age (www.who.int/dietphysicalactivity/en/).
- You may take part in a health and fitness appraisal.
- If you are over the age of 45 yr and NOT accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.
- If you have any further questions, contact a qualified exercise professional.

PARTICIPANT DECLARATION
If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that the community/fitness centre may retain a copy of this form for records. In these instances, it will maintain the confidentiality of the same, complying with applicable law.

NAME ______________________________ DATE ____________________

SIGNATURE ______________________________ WITNESS ____________________

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER ______________________________

If you answered YES to one or more of the questions above, COMPLETE PAGES 2 AND 3.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ at **www.eparmedx.com** before becoming more physically active.
- Your health changes - answer the questions on Pages 2 and 3 of this document and/or talk to your doctor or a qualified exercise professional before continuing with any physical activity program.

2018 PAR-Q+

The Physical Activity Readiness Questionnaire for Everyone

The health benefits of regular physical activity are clear; more people should engage in physical activity every day of the week. Participating in physical activity is very safe for MOST people. This questionnaire will tell you whether it is necessary for you to seek further advice from your doctor OR a qualified exercise professional before becoming more physically active.

GENERAL HEALTH QUESTIONS

Please read the 7 questions below carefully and answer each one honestly: check YES or NO.	YES	NO

2018 PAR-Q+

FOLLOW-UP QUESTIONS ABOUT YOUR MEDICAL CONDITION(S)

1.	**Do you have Arthritis, Osteoporosis, or Back Problems?** If the above condition(s) is/are present, answer questions 1a-1c — If **NO** ☐ go to question 2	
1a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
1b.	Do you have joint problems causing pain, a recent fracture or fracture caused by osteoporosis or cancer, displaced vertebra (e.g., spondylolisthesis), and/or spondylolysis/pars defect (a crack in the bony ring on the back of the spinal column)?	YES ☐ NO ☐
1c.	Have you had steroid injections or taken steroid tablets regularly for more than 3 months?	YES ☐ NO ☐
2.	**Do you currently have Cancer of any kind?** If the above condition(s) is/are present, answer questions 2a-2b — If **NO** ☐ go to question 3	
2a.	Does your cancer diagnosis include any of the following types: lung/bronchogenic, multiple myeloma (cancer of plasma cells), head, and/or neck?	YES ☐ NO ☐
2b.	Are you currently receiving cancer therapy (such as chemotheraphy or radiotherapy)?	YES ☐ NO ☐
3.	**Do you have a Heart or Cardiovascular Condition?** *This includes Coronary Artery Disease, Heart Failure, Diagnosed Abnormality of Heart Rhythm* If the above condition(s) is/are present, answer questions 3a-3d — If **NO** ☐ go to question 4	
3a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
3b.	Do you have an irregular heart beat that requires medical management? (e.g., atrial fibrillation, premature ventricular contraction)	YES ☐ NO ☐
3c.	Do you have chronic heart failure?	YES ☐ NO ☐
3d.	Do you have diagnosed coronary artery (cardiovascular) disease and have not participated in regular physical activity in the last 2 months?	YES ☐ NO ☐
4.	**Do you have High Blood Pressure?** If the above condition(s) is/are present, answer questions 4a-4b — If **NO** ☐ go to question 5	
4a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
4b.	Do you have a resting blood pressure equal to or greater than 160/90 mmHg with or without medication? (Answer **YES** if you do not know your resting blood pressure)	YES ☐ NO ☐
5.	**Do you have any Metabolic Conditions?** *This includes Type 1 Diabetes, Type 2 Diabetes, Pre-Diabetes* If the above condition(s) is/are present, answer questions 5a-5e — If **NO** ☐ go to question 6	
5a.	Do you often have difficulty controlling your blood sugar levels with foods, medications, or other physician-prescribed therapies?	YES ☐ NO ☐
5b.	Do you often suffer from signs and symptoms of low blood sugar (hypoglycemia) following exercise and/or during activities of daily living? Signs of hypoglycemia may include shakiness, nervousness, unusual irritability, abnormal sweating, dizziness or light-headedness, mental confusion, difficulty speaking, weakness, or sleepiness.	YES ☐ NO ☐
5c.	Do you have any signs or symptoms of diabetes complications such as heart or vascular disease and/or complications affecting your eyes, kidneys, **OR** the sensation in your toes and feet?	YES ☐ NO ☐
5d.	Do you have other metabolic conditions (such as current pregnancy-related diabetes, chronic kidney disease, or liver problems)?	YES ☐ NO ☐
5e.	Are you planning to engage in what for you is unusually high (or vigorous) intensity exercise in the near future?	YES ☐ NO ☐

2018 PAR-Q+

6. **Do you have any Mental Health Problems or Learning Difficulties?** *This includes Alzheimer's, Dementia, Depression, Anxiety Disorder, Eating Disorder, Psychotic Disorder, Intellectual Disability, Down Syndrome*

If the above condition(s) is/are present, answer questions 6a-6b — If **NO** ☐ go to question 7

6a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
6b.	Do you have Down Syndrome **AND** back problems affecting nerves or muscles?	YES ☐ NO ☐

7. **Do you have a Respiratory Disease?** *This includes Chronic Obstructive Pulmonary Disease, Asthma, Pulmonary High Blood Pressure*

If the above condition(s) is/are present, answer questions 7a-7d — If **NO** ☐ go to question 8

7a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
7b.	Has your doctor ever said your blood oxygen level is low at rest or during exercise and/or that you require supplemental oxygen therapy?	YES ☐ NO ☐
7c.	If asthmatic, do you currently have symptoms of chest tightness, wheezing, laboured breathing, consistent cough (more than 2 days/week), or have you used your rescue medication more than twice in the last week?	YES ☐ NO ☐
7d.	Has your doctor ever said you have high blood pressure in the blood vessels of your lungs?	YES ☐ NO ☐

8. **Do you have a Spinal Cord Injury?** *This includes Tetraplegia and Paraplegia*

If the above condition(s) is/are present, answer questions 8a-8c — If **NO** ☐ go to question 9

8a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
8b.	Do you commonly exhibit low resting blood pressure significant enough to cause dizziness, light-headedness, and/or fainting?	YES ☐ NO ☐
8c.	Has your physician indicated that you exhibit sudden bouts of high blood pressure (known as Autonomic Dysreflexia)?	YES ☐ NO ☐

9. **Have you had a Stroke?** *This includes Transient Ischemic Attack (TIA) or Cerebrovascular Event*

If the above condition(s) is/are present, answer questions 9a-9c — If **NO** ☐ go to question 10

9a.	Do you have difficulty controlling your condition with medications or other physician-prescribed therapies? (Answer **NO** if you are not currently taking medications or other treatments)	YES ☐ NO ☐
9b.	Do you have any impairment in walking or mobility?	YES ☐ NO ☐
9c.	Have you experienced a stroke or impairment in nerves or muscles in the past 6 months?	YES ☐ NO ☐

10. **Do you have any other medical condition not listed above or do you have two or more medical conditions?**

If you have other medical conditions, answer questions 10a-10c — If **NO** ☐ read the Page 4 recommendations

10a.	Have you experienced a blackout, fainted, or lost consciousness as a result of a head injury within the last 12 months **OR** have you had a diagnosed concussion within the last 12 months?	YES ☐ NO ☐
10b.	Do you have a medical condition that is not listed (such as epilepsy, neurological conditions, kidney problems)?	YES ☐ NO ☐
10c.	Do you currently live with two or more medical conditions?	YES ☐ NO ☐

PLEASE LIST YOUR MEDICAL CONDITION(S) AND ANY RELATED MEDICATIONS HERE: ______________________________

____

GO to Page 4 for recommendations about your current medical condition(s) and sign the PARTICIPANT DECLARATION.

2018 PAR-Q+

If you answered NO to all of the FOLLOW-UP questions (pgs. 2-3) about your medical condition, you are ready to become more physically active - sign the PARTICIPANT DECLARATION below:

- It is advised that you consult a qualified exercise professional to help you develop a safe and effective physical activity plan to meet your health needs.
- You are encouraged to start slowly and build up gradually - 20 to 60 minutes of low to moderate intensity exercise, 3-5 days per week including aerobic and muscle strengthening exercises.
- As you progress, you should aim to accumulate 150 minutes or more of moderate intensity physical activity per week.
- If you are over the age of 45 yr and **NOT** accustomed to regular vigorous to maximal effort exercise, consult a qualified exercise professional before engaging in this intensity of exercise.

If you answered **YES** to **one or more of the follow-up questions** about your medical condition:

You should seek further information before becoming more physically active or engaging in a fitness appraisal. You should complete the specially designed online screening and exercise recommendations program - the **ePARmed-X+ at www.eparmedx.com** and/or visit a qualified exercise professional to work through the ePARmed-X+ and for further information.

Delay becoming more active if:

- You have a temporary illness such as a cold or fever; it is best to wait until you feel better.
- You are pregnant - talk to your health care practitioner, your physician, a qualified exercise professional, and/or complete the ePARmed-X+ **at www.eparmedx.com** before becoming more physically active.
- Your health changes - talk to your doctor or qualified exercise professional before continuing with any physical activity program.

- You are encouraged to photocopy the PAR-Q+. You must use the entire questionnaire and NO changes are permitted.
- The authors, the PAR-Q+ Collaboration, partner organizations, and their agents assume no liability for persons who undertake physical activity and/or make use of the PAR-Q+ or ePARmed-X+. If in doubt after completing the questionnaire, consult your doctor prior to physical activity.

PARTICIPANT DECLARATION

- All persons who have completed the PAR-Q+ please read and sign the declaration below.
- If you are less than the legal age required for consent or require the assent of a care provider, your parent, guardian or care provider must also sign this form.

I, the undersigned, have read, understood to my full satisfaction and completed this questionnaire. I acknowledge that this physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if my condition changes. I also acknowledge that the community/fitness center may retain a copy of this form for records. In these instances, it will maintain the confidentiality of the same, complying with applicable law.

NAME ______________________________ DATE ______________________________

SIGNATURE ______________________________ WITNESS ______________________________

SIGNATURE OF PARENT/GUARDIAN/CARE PROVIDER ______________________________

For more information, please contact

www.eparmedx.com

Email: eparmedx@gmail.com

Citation for PAR-Q+

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The PAR-Q+ was created using the evidence-based AGREE process (1) by the PAR-Q+ Collaboration chaired by Dr. Darren E. R. Warburton with Dr. Norman Gledhill, Dr. Veronica Jamnik, and Dr. Donald C. McKenzie (2). Production of this document has been made possible through financial contributions from the Public Health Agency of Canada and the BC Ministry of Health Services. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada or the BC Ministry of Health Services.

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APPENDIX C

HEAD TRAUMA AND SPORTS QUESTIONNAIRE

Participant Number: ______________ **Date: ______________**

Concussions

Participants were provided the following definition of concussion:

> "Some people have the misconception that concussions only happen when you black out after a hit to the head or when the symptoms last for a while. But, in reality, a concussion has occurred anytime you have had a blow to the head that caused you to have symptoms for any amount of time. These include: blurred or double vision, seeing stars, sensitivity to light or noise, headache, dizziness or balance problems, nausea, vomiting, trouble sleeping, fatigue, confusion, difficulty remembering, difficulty concentrating, or loss of consciousness. Whenever anyone gets a ding or their bell rung, that too is a concussion"

Based on this definition, participants were asked to state approximately how many total concussions they have had during their life.

After having this definition read to you, please estimate the total number of concussions you believe you have suffered throughout your lifetime.

Total # of concussions: ________

Please estimate to the best of your ability when each concussion occurred, starting with the most recent. If you have had more than 4, please continue to write below the table:

Concussion	Month	Year
1		
2		
3		
4		

Sports

After having the following definitions read to you, please complete the two tables on the next page to the best of your ability.

- Non-contact-sports → Sports that have limited physical contact that is incidental and not required by the rules.

  E.g.: baseball, softball, swimming, track and field, and volleyball.

- Contact-sports → Sports that have a considerable amount of physical contact between opponents that is not incidental, but intentional. Sports that do or do no not require physical contact by the structured rules are included.

  E.g.: basketball, soccer, field hockey, lacrosse (men's and women's), wrestling, football, ice hockey, and rugby.

- Organized Sport → A sport that involves officiated/judged competition.

CONTACT-SPORTS

Previous Sport(s)

Please fill in the following table with the organized contact-sports you ***previously participated*** in. If you have had participated in more than 6 organized contact-sports, please continue to write below the table:

Sport	How long (months) did participation in this sport last?	How long (hours per week) did you participate in this sport?	When (month and year) did you stop playing this sport?
E.g.: Basketball	9 months	10hr/wk	October 2016

Current Sport(s)

Please fill in the following table with the organized contact-sports you ***currently participate*** in. If you currently participate in more than 6 organized contact-sports, please continue to write below the table:

Sport	How long (months) have you participated in this sport?	How long (hours per week) do you participate in this sport?
E.g.: Soccer	45 months	15hr/wk

NON-CONTACT-SPORTS

Previous Sport(s)

Please fill in the following table with the organized non-contact-sports you ***previously participated*** in. If you have had participated in more than 6 organized non-contact-sports, please continue to write below the table:

Sport	How long (months) did participation in this sport last?	How long (hours per week) did you participate in this sport?	When (month and year) did you stop playing this sport?
E.g.: Swimming	9 months	10hr/wk	October 2016

Current Sport(s)

Please fill in the following table with the organized non-contact-sports you ***currently participate*** in. If you currently participate in more than 6 organized non-contact-sports, please continue to write below the table:

Sport	How long (months) have you participated in this sport?	How long (hours per week) do you participate in this sport?
E.g.: Volleyball	45 months	15hr/wk

APPENDIX D

SYMPTOM CHECKLIST

Participant Number: ______________ **Date: ______________**

For your most recent concussion, please complete the following symptom checklist to the best of your ability. Please circle how severe each symptom was/is for each segment of time.

1 = none, 2 = mild, 3 = moderate, 4 = severe

Symptom	48 hours post-concussion	3-14 days post-concussion	15 days through 1-month post-concussion	2 - 3 months post-concussion	Persisting Symptoms (symptoms continued more than 3 months post-concussion or did not resolve)
Nausea	1 2 3 4	1 2 3 4	1 2 3 4	1 2 3 4	1 2 3 4
Vomiting	1 2 3 4	1 2 3 4	1 2 3 4	1 2 3 4	1 2 3 4
Appetite Changes	1 2 3 4	1 2 3 4	1 2 3 4	1 2 3 4	1 2 3 4
Unplanned Weight Change	1 2 3 4	1 2 3 4	1 2 3 4	1 2 3 4	1 2 3 4

If you do not remember any of these time segments, please indicate why:

APPENDIX E

SEVEN-DAY PHYSICAL ACTIVITY RECALL

The Seven-Day Recall

PAR#: 1 2 3 4 5 6 7 Participant____

Interviewer________________Today is________________ Today's Date_____

1. Were you employed in the last seven days? **0. No** (Skip to **Q#4**) 1. **Yes**
2. How many days of the last seven did you work? ____ days
3. How many total hours did you work in the last seven days? ____ hours last week
4. What two days do you consider your weekend days? ________ ________ (mark days below with a squiggle)

WORKSHEET **DAYS**

	SLEEP	1 __	2 __	3 __	4 __	5 __	6 __	7 __
MORNING	**Moderate**							
	Hard							
	Very Hard							
AFTERNOON	**Moderate**							
	Hard							
	Very Hard							
EVENING	**Moderate**							
	Hard							
	Very Hard							
Total Min Per Day	**Strength:** **Flexibility:**	_____	_____	_____	_____	_____	_____	_____

4a. Compared to your physical activity over the past three months, was last week's physical activity more, less or about the same?
1. More
2. Less
3. About the same

Worksheet Key:	Rounding:	
An asterisk (*) denotes a work-related activity.	10-22 min.=.25	1:08-1:22 hr/min.=1.25
A squiggly line through a column (day) denotes a weekend day.	23-37 min.=.50	
	38-52 min.=.75	
	53-1:07 hr/min. =1.0	

INTERVIEWER:

Please answer questions below and note any comments on interview.

5. Were there any problems with the 7-Day PAR interview? 0. No
   1. Yes (If yes, please explain.)

   Explain any problems you had with this interview:

   ____

   ____

   ____

   ____

6. Do you think this was a valid 7-Day PAR interview? 0. No
   1. Yes

7. Please list below any activities reported by the subject which you don't know how to classify.

   ____

   ____

   ____

   ____

8. Please provide any other comments you may have in the space below.

   ____

   ____

   ____

   ____

Introduction

The next set of questions that I will be asking you refers to the physical activities you've engaged in during the past week.

Work

I am going to start by asking you a few questions about your employment. (*Ask employment questions on top of PAR worksheet.*)

Weekend Days

What 2 d of the week do you consider to be your weekend days? Most people consider Sat. and Sun. to be their weekend days, but it may be different for you.

Record the 2 weekend days in the space provided on the worksheet and draw squiggly lines through the 2 weekend days.

Sleep

Now I'd like to look at the time you spent sleeping in the past week. By sleeping, I mean the time you went to bed one night and the time that you got out of bed the next morning. You may not necessarily have been asleep the entire time you were in bed. You may have been reading or watching television.

Today is (i.e., Monday), so yesterday was (i.e., Sunday).

What time did you go to bed (Sunday) night and get up (Monday) morning?

Do this for each day of the 7-d recall. Write down days of week and sleep times reported by the participant in the space provided on the top of the worksheet. Calculate total time spent sleeping after completing the interview.

Physical Activity

I am going to ask you about the physical activities you engaged in during the past 7 d, starting with yesterday and going back 7 d. In doing so, please remember, this is a recall of actual activities for the past week, not a history of what you usually do.

We are not considering light activities, such as desk work, standing, light housework, softball, and bowling. We are considering occupational, household, recreational, and sports activities that make you **feel** similar to how you feel when you are walking at a normal pace. For example, slow stop-and-go walking such as window shopping, is **not** included; however, walking at a normal pace to do an errand is included.

Intensity Guidelines

I will ask you to categorize the intensity of each physical activity you do into one of three groups, moderate, hard, or very hard:

- The moderate category is similar to how you **feel** when you're **walking at a normal pace**.
- The very hard category is similar to how you **feel** when you are **running**.
- The hard category just falls in between.
- In other words, if the activity seems harder than walking but not as strenuous as running, it should go in the hard category.

Segments of the Day

I am going to ask you about the physical activities you engaged in during three segments of the day, which includes morning, afternoon, and evening. Morning is considered from the time you get up in the morning to the time you have lunch; afternoon is from lunch to dinner; and evening is from dinner until the time you go to bed.

Setting the Stage

Getting people to think about their day in general will help them remember all of their activities. Always spend some time "setting the stage" for each day.

Today is (i.e., Monday), so yesterday was (i.e., Sunday). Think about what you did (Sunday) morning. **Where were you? Think about what you usually do. Did you do anything unusual?** Did you do any physical activity (Sunday morning)?

Duration

The activity in question should be performed for a total of 10 min, intermittently or continuously, during one segment of the day, morning, afternoon, or evening (except for strength and flexibility, in which the total amount of minutes is recorded)

How long did you do that activity?

Make sure that the activity excludes the time that they stood still or took breaks.

How much of that time was spent standing still or taking **breaks**?

Intensity

Always refer to intensity guidelines: "Did that activity feel similar to how you feel when you are walking or running or is it somewhere in between?"

Did that activity make you feel similar to how you feel when you are walking or running, or is it somewhere in between? (How would you rate the intensity of that activity? Did it feel similar to how you feel when you walk or run or somewhere in between? Keep in mind that a moderate intensity feels similar to walking at a normal-to-brisk pace, and very hard feels similar to running.) Think about what you did **in general** (Sun) afternoon. Did you do any physical activity?

Strength and Flexibility

Record the total number of minutes spent doing strength activities and the total minutes spent doing flexibility activities separately for each day. Make sure that the activity excludes the time during which the participant or stood still or took breaks.

Now I am going to ask you about activities you might do for building strength or improving flexibility. Strength activities include push-ups, pull-ups, sit-ups, lifting free weights, and using weight machines. Flexibility activities include holding stretches for several seconds and yoga. Did you do any strength or flexibility activities? How many minutes did you spend on each? (*Record separately at the bottom of the worksheet.*)

At the End of Each Day Ask

Are there any physical activities **that you might have forgotten**? Did you do any physical activity at work? any other recreational or sport activities? housework or gardening? Were there any other walks that you might have taken?

On the Last Day of Recall Ask

Take a moment to think back over the course of the week and think of any activities that you may have forgotten.

Last Question

The last question I am going to ask you is, "Compared to your physical activity over the past 3 mo, was last week's physical activity more, less, or about the same?"

Record answer on bottom of worksheet.

Summary

- Ask about the subject's physical activity during each segment of the day for each of the 7 d of the recall.
- Start with the previous day and go backwards. Record each day's recall in turn.
    a. Set the stage by having participants recall what they did in general.
    b. Record separately for the morning, the afternoon, and the evening.
    c. Ask if they missed any activities.
- After each day be sure to ask about strength and flexibility and about any activities that may have been forgotten.
- Record everything on the worksheet.
- Record on the worksheet the time and the intensity of the activity. Make sure to record the activity on the worksheet in the correct segment of the day.
- Complete the 7-Day PAR interview by asking the question at the bottom of the worksheet regarding physical activity over the past 3 mo.
- On the back of the worksheet, answer the questions and note anything the participant stated that might be helpful in interpreting the data.
- It is OK for the subject to add or change a previous report later in the interview.

Par Review Checklist

Interviewer: __________
Reviewer: __________
Date: __________
Interviewer Techniques
Yes or No
Comments

1. Ask questions about work schedule. ______
2. Defines "sleep" correctly. ______
3. Reviews sleep habits, beginning with previous night. ______
4. Explains intensity guidelines (Walk = moderate, run = very hard.) ______
5. Explains that stop-and-go walking is not included if intensity is not at least moderate.
6. Asks in general what subject was doing each day, using context cues for better recall.
7. Asks about activities that may have been forgotten for each day. ______
8. Asks about strength and flexibility activities for each day. ______

9. Asks which days are considered weekends. ______
10. Asks separately about morning, afternoon, and evening activities. ______
11. Clarifies which activities are job-related. ______
12. Prompts subject to define intensity level by referring "zero intensity" guidelines. ______
13. Makes clear the length of activities. ______
14. Prompts for any "breaks" taken. ______
15. Asks about any activities for the week that may have been forgotten. ______

Scoring

1. Puts times in correct places on worksheet. ______
2. Records activities that add up to at least 10 min in one intensity category during one segment of day (i.e., three 5-min "bouts" of activity = 15 min) ______
3. Marks weekend days. ______
4. Marks job-related activities. ______
5. Uses correct arithmetic. ______
6. Uses correct rules for rounding of values. ______
7. Compare scoring of interviewer and reviewer. (Note reasons for discrepancies.) ______

Reviewers Comments

Strengths:

Needs improvement:

The authors gratefully acknowledge Neville Owen and Steve Blair for their helpful comments.

CALCULATIONS

The number of hours spent in sleep and different activity levels are obtained. Time spent in sleep (1 MET), light (1.5 METs), moderate (4 METs), hard (6 METs), and very hard (10 METs) activities for the past 7 d are multiplied by their respective MET values and then summed (9). An estimate of total kilocalories of energy expenditure per day is calculated, as in the following example.

EXAMPLE

Data from the 7-Day Recall:

Sleep:	60.0 h × 1 MET = 60 kcal/kg
Light:	99.5 h × 1.5 METs = 149 kcal/kg
Moderate:	3.5 h × 4 METs = 14 kcal/kg
Hard:	2.5 h × 6 METs = 15 kcal/kg
Very Hard:	2.5 h × 10 METs = 25 kcal/kg

Total weekly energy expenditure = 263 kcal/kg/wk

Total daily energy expenditure = 263 kcal/kg/wk ÷ 7 d/wk = 37.8 kcal/kg/d

For a 70-kg individual: 37.8 kcal/kg/d × 70 kg = 2646 kcal/d

APPENDIX F

EMAIL SCRIPT

Investigators in the School of Kinesiology at Ball State University need research subjects for their study *Long-term effects of head trauma in contact-sport athletes on autonomic function*

IRB Approval _______

Who:

- Healthy Adults ages 18-40
- Non-smokers
- Without any known cardiovascular, pulmonary, or metabolic disease
- No medications that alter autonomic, metabolic, or cardiovascular function

What:

- Expected time commitment is a one-time visit to the laboratory lasting 2 hours
- You will be asked to fast for 12 hours and refrain from vigorous exercise prior to the data collection testing session.

Where:

- Health and Physical Activities Building, Ball State University
- Parking is available if coming from off campus.

Participants will receive body composition testing results.

If you are interested in participating in this study or would like more information regarding this study please email iepl@bsu.edu

APPENDIX G

SOCIAL MEDIA RECRUITMENT

Twitter:

BSU investigators need participants to study head trauma effects on autonomic function. Looking for apparently healthy males & females 18-40yrs, previously concussed or not concussed, to visit HP 307 once for 2hrs. More information can be found at https://bit.ly/2ClFS5t.

Facebook:

RESEARCH PARTICIPANTS NEEDED!!
Who:

- Healthy Male & Female Adults ages 18-40
- Non-smokers
- Without any known cardiovascular, pulmonary, or metabolic disease
- No medications that alter autonomic, metabolic, or cardiovascular function
- Looking for individuals both previously concussed and not previously concussed

No eating 12 hours before data collection and no exercise, caffeine, or alcohol 24 hours before data collection.
All participants will also receive body composition testing results.
Data will be collected during a one-time visit the Integrated Exercise Physiology Laboratory (HP 307) lasting 2 hours.
Interested or want to find out more? Email Carley Shannon, graduate assistant in the Integrative Exercise Physiology Laboratory, at cashannon@bsu.edu
This study is being conducted under the supervision of Dr. Andrew Del Pozzi. IRB#_________

APPENDIX H

RECRUITMENT FLYER

Concussion and Head Trauma Research Study

Healthy men & women needed to participate in a study investigating the effects of concussions and head trauma on blood pressure, heart rate, and respiratory rate.

Qualifications

- ☐ Healthy, non-smoking men & women, 18-40 years of age
- ☐ No medications that alter autonomic, metabolic, or cardiovascular function
- ☐ No known cardiovascular, pulmonary, or metabolic disorders
- ☐ Looking for individuals both previously concussed and not previously concussed

Data will be collected during a one-time visit lasting 2 hours

All participants will also receive body composition testing results

No eating 12 hours before data collection.
No exercise, caffeine, or alcohol 24 hours before data collection.

10 participants will be accepted in each of the 3 groups: non-contact-sport athlete and never concussed; contact-sport athlete and never concussed; and contact-sport athlete with previous concussion(s). All groups are first come, first serve until they are filled.

For more information, call (765) 285-4249 or email iepl@bsu.edu

IRB Approval#____________